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DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 1983

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

NINETY-SEVENTH CONGRESS

SECOND SESSION

Part 2—(Pages 1–692)

CONGRESSIONAL WITNESS
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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CONTENTS

WEDNESDAY, FEBRUARY 3, 1982

Page
Congressional witness 1
Department of Health and Human Services 11

MONDAY, MARCH 2, 1982

Department of Health and Human Services:

Centers for Disease Control 57
Health Services Administration 139

TUESDAY, FEBRUARY 23, 1982

Department of Health and Human Services:
National Institutes of Health:

National Institute of Neurological and Communicative Disorders and Stroke 189
National Institute of Allergy and Infectious Diseases 219
National Institute of General Medical Sciences 255
National Institute of Child Health and Human Development 283
National Eye Institute 307
National Institute of Environmental Health Sciences 335
National Institutes of Health 371
National Cancer Institute 431
National Heart, Lung, and Blood Institute 473
National Institute of Dental Research 527
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases 549

MONDAY, FEBRUARY 22, 1982

Department of Health and Human Services:
Public Health Service:

National Institute on Aging 585

National Institutes of Health:

Division of Research Resources 617
John E. Fogarty Center for Advanced Study in the Health Sciences 647
National Library of Medicine 663
Administration 681

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 1983

WEDNESDAY, FEBRUARY 3, 1982

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, D.C.

The subcommittee met at 1:35 p.m., in room 1114, Everett McKinley Dirksen Senate Office Building, Hon. Harrison H. Schmitt (chairman) presiding.

Present: Senators Schmitt, Abdnor, and Burdick.

CONGRESSIONAL WITNESS

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. Good afternoon, ladies and gentlemen. The hearing will come to order.

Welcome, Senator Denton, to our deliberations. And if you will allow me, Senator, I will proceed with an opening statement and then invite you to address the subcommittee.

This, in fact, is the start of our fiscal 1983 hearing process.

I believe it is appropriate to view these hearings and others as they come down the line as a continuation of the work begun by this subcommittee last year. In the preceding 12 months, our subcommittee started the difficult task of reducing the growth in the very large portion of the budget under our jurisdiction.

I am glad to report that we were able to make substantial cuts in Federal spending, in what we believe was unnecessary or excessive Federal spending, incorporated in the Senate contribution of the continuing resolution for 1982, while still assuring continuation of essential services to the needy. It was a difficult task, but the subcommittee, I believe, can be pleased with the results of its work.

The subcommittee also began the equally tough job of reviewing the programs for their effectiveness. This took up a good deal of our time in fiscal 1982 hearings.

It has been also useful in preparing the bills that have been sent to the subcommittee. I believe we were able to make some far-reaching funding choices among programs based on their ability to serve the Nation's needs, and how well they had served or not served those needs in the preceding years. The crucible of experience was the essence of our activity.

In this connection, we put our support behind programs providing vocational training on the simple ground that these offer a more promising means for putting people to work in useful jobs than do programs which stress make-work activities.

In the area of health, we made clear our belief that biomedical research is an important priority and that the work of the National Institutes of Health should be continued and strengthened if we are ever going to ultimately solve the problem of rising health-care costs. We can only expect to solve this problem in the future through prevention of sickness rather than ever-increasing costly treatment.

In the same vein, it is our belief that programs in such areas as immunization, VD control, rural health care, training of health professionals, refugee resettlement, aid to the elderly, compensatory education, education of the handicapped, and assistance to low-income college students are also high priorities which should be supported.

Our subcommittee also strengthened the effort to root out fraud, waste, and abuse in programs under our jurisdiction, and strived to reduce funding in such less essential areas as administrative overhead and consultants.

This is the base on which the subcommittee will resume its activities in fiscal 1983. The year ahead will give the subcommittee the opportunity to review its work of the past 12 months to determine where improvements can be made. In this connection, the subcommittee will be essentially and especially interested in how the States are implementing the new block-grant programs in health, education, and community services.

A major and continuing concern of the subcommittee will be the rising cost of the entitlement programs in our bill. Consider these figures: Of the total of $84.5 billion available for 1982 Labor-Health and Human Services and Education programs, some $57 billion, or 67 percent, is needed for these entitlement programs over which the subcommittee has control. This leaves only $27 billion for essential programs over which the subcommittee can exercise discretion.

The entitlements are a constant and rapidly worsening drain on the funds allocated to our bill and also contribute significantly to the budget deficit. This is a bad situation, and I am glad the President will present a package of entitlement reforms in conjunction with his forthcoming fiscal 1983 budget.

But the effort must not stop there. The congressional authorizing committees which have jurisdiction in this area must take up the President's challenge and act this year to reduce the rate of growth of the entitlement programs. It will not be easy, but it must be done.

While doing this, the essential safety net character of the programs must be preserved so that those persons who, through no fault of their own, have become entangled in the edges of the safety net can be served. However, we need to find alternatives to Federal assistance.

Certainly, in many of these areas, the subcommittee's efforts to encourage vocational education will be critical in giving the option to people now entangled in the safety net.

Our committee will be watching the authorizing committees very closely. As many are aware, we have worked out and may be prepared sometime in the future to take our own initiatives if, in fact, the authorizing committees are unable to do so.

The Labor, Health and Human Services and Education Subcommittee has a full schedule of activities planned in the months to come. I look forward to building on the constructive start that was made by the subcommittee in fiscal 1982.

Today, the subcommittee will review a number of programs which were authorized last year, but still have not been funded. Before the subcommittee decides whether funding should be made available, it wishes to have a better idea of what the programs would do. That is the purpose of today's hearing.

Our first witness is Senator Jeremiah Denton of Alabama who is here to tell us about the adolescent family life program.

Senator Paula Hawkins was scheduled to testify on behalf of the proposed tuberculosis control program, but we regret to learn that, for health reasons, she cannot be with us today. We certainly wish her a speedy recovery. Her testimony in full will be included in the record of our hearing.

Jerry, it is great to have you with us today. I know it seems as if it has taken forever to get to this position, but, unfortunately, there are certain procedures that even a subcommittee like this has to follow. We are happy that we finally have a chance to hear your case.

Senator Denton.

STATEMENT OF HON. JEREMIAH DENTON, U.S. SENATOR FROM ALABAMA

Senator DENTON. Thank you, Mr. Chairman.

I would like to thank you not only for your friendly remarks, but for the opportunity to appear here. And as you say, it has been a long time coming. It has always been a pleasure to work with you. And as you know, my respect for you has been expressed in broader forums than in this committee hearing room. I have praised your work as Senator and senatorial qualities in public forums nationally.

I would like to take this opportunity to compliment you now on your diligent efforts to shape an equitable appropriations bill during what all of us would agree are difficult times. My comments address the adolescent family life program which was approved by Congress last year.

As chairman of the Subcommittee on Aging, Family, and Human Services, having adolescent pregnancy as an area under my legislative responsibilities, I proposed the adolescent family life bill which, I am happy to report, passed unanimously in the Labor and Human Resources Committee.

As you know, the adolescent family life program is authorized by Congress to receive $30 million for each of the years 1982 through 1984. The Office of Management and Budget has told me they will recommend a 1982 funding level of approximately $11 million and $16 million in fiscal year 1983.

I am here to urge the chairman and the subcommittee to allocate at least this sum to continue adolescent pregnancy programs begun in 1978 and to initiate demonstration projects found to be required to alleviate a social problem of significant importance, respecting the drain on Federal dollars.

I earnestly hope in the few minutes available to me today, I am able to impart to you, Mr. Chairman, the sum of the findings resulting from months of study by the Labor and Human Resources Committee which resulted in the unanimous vote in favor of this program. This program approved by Congress not only continues worthwhile programs for pregnant adolescents, but offers new family-oriented approaches to help America's youth by addressing the problem of adolescent sexual activity itself, as well as its consequences.

With increasing numbers of adolescents having full sexual relations at earlier ages outside of marriage, and a growing rate of adolescent mothers giving birth outside of wedlock, we need, obviously, to try innovative approaches. Professionals and parents have repeatedly informed the Subcommittee on Aging, Family, and Human Services that such approaches should include projects which educate and counsel young people on the physiological, psychological, and emotional consequences of such sexual activity.

The adverse side effects of artificial contraception alone include possible cervical cancer, greater risk of stroke, blood clotting, anemia, infertility, high blood pressure, and the development of depressive personality changes.

The impact of the adverse side effects of artificial contraception is heightened in the adolescent stage. And the result of this and other adverse effects has direct and in many cases unidentified economic impacts on the Federal budget.

The adolescent family life program does not accept the position that premarital adolescent sexual activity is inevitable. That particular argument is rooted in hopelessness—the Federal Government should offer something more to today's young people. Humankind is more than animal in nature. Most of our youth know that. And many are heroically well-behaved.

The adolescent family life program is designed to accommodate and elicit that kind of behavior. Through the promotion of prevention services, it would encourage family-centered sexual education and responsibility-oriented counseling.

I have just been given, before coming into the room, an example of the kind of approach which could be built under this legislation—a multistate project currently under development, which would focus on the preventive aspects of the adolescent family life bill. The project is entitled, "Family Life, An Alternative National Curriculum."

Universities and public school districts in three Western States, including New Mexico, Utah, and California, would work with families in implementing this properly. Dr. Terrance D. Olson, professor of family science at Brigham Young University, is developing the program, working closely with people in New Mexico, including Dr. David Darling, dean of the college of education, University of New Mexico, Dr. Mary Margaret Smith, acting chairperson in the department of home economics, University of New Mexico, and Pat Baca, a counselor at Del Norte High School in Albuquerque.

The objective of this project is to conduct family-centered, family-life curriculum designed to teach responsible living, economic education, and sexual decisionmaking in the context of the family unit.

The foundation of this program is the prevention of self-destructive behaviors which teenagers too often fall prey to in the current education and social climates to which they are exposed.

I met with Dr. Olson as I came in the room. I think he has some excellent ideas. I offer this as an example of the kinds of programs which might be built as a result of this legislation.

You have asked what the goals and purposes are. Another purpose of the adolescent family life program is to emphasize that taxpayer-support programs should produce services to unmarried pregnant girls. This is made clear in the program's requirement that at least two-thirds of the money for demonstration projects must be used for service to pregnant adolescents.

One of the main thrusts of the program is to present the positive alternative of adoption to unwed, adolescent, and expectant parents. To some high school age girls, having a baby has become a status symbol. The consciousness of status as a principal criterion gradually disappears when the responsibilities of single-parenthood become a reality to the unwed adolescent mother.

Adoption, then, can often be the best option for both the child and the mother. The adolescent family life program will insure that counselors fully explore the positive option of adoption with their clients so that expectant adolescents make an informed choice for the future of their babies.

Federal programs in this area should also provide information to pregnant adolescents on the proper nurturing of the children they carry. AFL demonstration projects would develop programs to insure that young, expectant mothers have the knowledge necessary to deliver strong, healthy babies.

They would also assist adolescent, expectant parents to continue their education, provide job training, and postnatal care if they are determined to raise the child themselves.

Mr. Chairman, it is the family that this administration and this Congress wish to support. Federal programs should not forget that the family's prime purpose is to provide and shape the future generation. As a general rule, no other institution can replace the family in the essential task of rearing children with all of the implications which rearing children entail.

In addition to demonstration service projects, the adolescent family life program will provide research grants to investigate the consequences of adolescent sexual relations, pregnancy, and childrearing. Research grants would also identify the means to resolve or alleviate the consequences of these activities.

The cost of adolescent pregnancy is high in taxpayer dollars, and even higher in affected lives. With increasing numbers of adolescent girls becoming pregnant each year, this toll mounts higher.

The Federal share for each adolescent family life demonstration project, though, will decrease each year after the second year of operation. The aim is to stimulate and involve private and local public funding with a phaseout of all Federal assistance over a 5-year period.

In terms of the Federal budget, we are not talking about a great deal of money here. But in terms of potential for helping America's youth and helping the drain on the budget, on Federal spending, we are talking about a positive step forward; a step grounded in the hope that problems are solvable.

I would like at this point, Mr. Chairman, to submit a partial list of organizations which endorse the family life program. For the record, these are:

The National Urban League; the National Catholic Conference of Bishops; the National Conference of Catholic Charities; the National Committee for Adoption; the Kennedy Foundation; the American Life Lobby; the National Right to Life; the American Citizens Concerned for Life; the National Alliance for Optional Parenthood; the March of Dimes; the United Families of America; the National Association of Evangelicals; and the World Organization for the Ovulation Method.

Mr. Chairman, I respectfully urge the subcommittee to recommend the necessary appropriations for the adolescent family life program to enable it to commence operation. I look forward to working with you and other members of this subcommittee in this matter.

I want to thank you again, sir.

Senator SCHMITT. Thank you, Senator Denton.

Senator, your testimony touched, in many ways, on dealing with the problem of adolescent pregnancy. As I understand it, the New Mexico, BYU, and California program is going to focus on the prevention aspects of the act.

What is the balance you see we ought to place on prevention versus treatment?

Senator DENTON. Well, the requirements for the bill include the services of prevention and care. And they also include a research portion. Not more than one-third of the funding to grantees from the Department, as I understand it—and I wish to be corrected on this if I make an error—is allocated for research, which I can discuss later.

Within the services portion, not more than one-third of the remaining moneys can be allocated to prevention. And the remainder would be for care.

Now, the Department of Health and Human Services has not written all the regulations for this act. And I will have to ask the Department if I have generally characterized that situation correctly.

Senator SCHMITT. We will be getting some information from the Department in a few minutes.

Senator DENTON. But if you wish to have a more or less quantitative financial answer, if that is what you are after, Mr. Chairman, I believe there is a great untapped reservoir of potential in terms of prevention by virtue of the various parameters which this program presents.

We do emphasize the involvement of the family unlike any existing program. And we even encourage counseling by the people associated with the denominational religion of the adolescent involved.

In other words, the prevention component stresses more than just the application of contraceptives. On the contrary, we try to get at the factors relating to the decision on the part of the adolescent, 13- or 14-year-old girl, to commit herself to an early sexual relations phase in her life. This aspect, I believe, is one which has been underemphasized and one which in this program, in the services portion, represents some promising potential.

We have a good bit of evidence in previous research programs to indicate that this is the case. For example, a program at Johns Hopkins University, entitled "The New Futures Program," indicates that services can reduce repeat pregnancies. We have evidence from research that teens from families with good communications are less likely to initiate early sexual activity. By encouraging communication, we would hope that the consequences of the resulting decision would be favorably effective.

And we find, too, that if they have better communications with their families and are committed to be sexually active anyway, these adolescents, in that category are more likely to make consistent use of contraceptives.

So we are not starting from scratch with our proposal. We really have, I believe, the weight of commonsense and the weight of demonstrated need on the side of this type of preventive approach. But keep in mind, Mr. Chairman, we are not anticipating or boasting of a wholesale reduction in the rate of incidence of sexual activity and abortion pregnancy.

It is intended principally to provide for demonstration projects leading to more effective programs than those which have been used so far without such apparent efficacious effects as to continue with just one approach.

Senator SCHMITT. Senator, I don't think, though, that the subcommittee or anyone should expect to see, in the 5-year period of this program, a large quantitative change in the number of adolescent pregnancies.

What I gather you and the supporters of this are indicating is that you are trying to lay the groundwork for a spontaneous change occurring as the ideas generated by this program permeate the State and local level and, more importantly, the family. Is that a correct summary of the situation as you see it?

Senator DENTON. Well, I think, Mr. Chairman, first of all, the parameters here are reasonably broad, allowing a good deal of initiative in the precise type of approach taken by individual grantees. We expect that among those demonstration projects considered for funding that we will develop several approaches each of which is efficacious and superior to those currently in practice. And in the long term you would see a decrease of the adverse side effects and consequences of adolescent sexual relations.

Senator SCHMITT. Senator, you have led me into my next question which is related to the general question before the Congresswith regard to return or the transfer of responsibilities of the social programs of various kinds to the States, while the Federal Government may take over full responsibility for assistance to the sick and the elderly.

In that context, if the Congress were to increase the appropriation and earmark portions of that appropriation under the maternal and child health services block grant, rather than create a new categorical program under this particular account, what would be your view of the effect of that operation?

Senator DENTON. Well, let me direct myself to the question of the separateness of the categorical program at this point and acknowledge that the administration did originally propose to include the antecedent program of this one, an adolescent pregnancy program, in the block grant.

I had to address myself to that program as chairman of the subcommittee. As we looked into it, we found that the former program run by the Office of Adolescent Pregnancy Programs had barely gotten off the ground. Only 23 projects had been funded for more than a year—less than 1 in every State.

We concluded that it would have been unreasonable to expect those States which had little knowledge of the dimensions of the problem of adolescent sexual relations or experience with programs which successfully dealt with the situation to undertake such a venture with constructive results.

The administration agrees totally with us, and quite enthusiastically supports the adolescent family life program.

Senator SCHMITT. Senator, we are going to move on and hear details from the administration. We may have a few more questions for the record. We appreciate very much your sharing your insights with the subcommittee. And we will proceed from that.

Senator DENTON. Thank you, Mr. Chairman.

[The statement follows:]

STATEMENT OF HON. PAULA HAWKINS, U.S. SENATOR FROM FLORIDA

Mr. Chairman, it is a pleasure to appear before the Senate Appropriations Subcommitte on Labor, Health and Human Services, and Education to testify in support of appropriations for tuberculosis control. I appreciate your granting me the opportunity to testify.

As you may know, I have filed an amendment to the Labor, Health and Human Services, Education appropriations bill to appropriate $9 million, the amount authorized previously by the 97th Congress for a categorical tuberculosis grant program to be administered by the Center for Disease Control. I want to share with you the reasons why I feel it is essential that funding for tuberculosis control must be restored.

Federal funding for TB control is not a new idea. In 1959, the U.S. Public Health Service and the National Tuberculosis Association brought together a group of national leaders in public health and tuberculosis control at the Arden Conference. As a result of this conference, the Federal Government first initiated a program of special project grants. Later, in the 1970's, a block-grant program replaced the special grants program as the source of Federal funding for tuberculosis control. In fact, that program just expired 4 months ago.

Federal health officials now believe that tuberculosis has reemerged as a serious health problem, particularly among children. For example, the Public Health Service recently reported that last year, for the first time in 18 years, the number of new cases of tuberculosis in the United States exceeded those in the preceding year. This is only the second time since the Center for Disease Control has kept statistical data on tuberculosis that the number of reported cases has increased.

In addition, the Centers for Disease Control report that the number of tuberculosis cases increased in 30 States and the District of Columbia last year. The steady 35-year decline in reported TB cases has reversed.

Especially alarming is the increased number of children who are now catching this deadly disease. In 1979, a total of 1,620 new cases of tuberculosis were reported among children, 900 of these children were under 5 years of age—an increase of 18 percent over 1978. This increase in the number of tuberculosis cases among children is considered significant because it documents that this infectious disease is being transmitted and is not under control. Tuberculosis is especially dangerous for children. As officially stated by the Public Health Service: "Tuberculosis is a serious disease of children because of the potential complications of meningitis which may lead to severe brain damage and death. Because of its severity, special efforts should be made toward eliminating tuberculosis among children."

TB does not just strike children. More than 15 million Americans are now infected with dormant forms of this disease. However, decreased immunity, due to old age, illness, or lack of proper nutrition, will activate dormant infections. And because TB symptoms—bad cough, weight loss, fever, and malaise—are often ignored, any outbreak of this highly infectious disease will spread rapidly.

In fact, a new outbreak could occur at any time. A report prepared by the Subcommittee on Health and Environment of the House Energy and Commerce Committee states: "Large numbers of infectious persons are not being effectively treated, and transmissions continue to occur."

Now, some believe that the TB control should be funded out of an overall preventive health block grant. Yet those Federal officials who believe this should remember that TB usually strikes the indigent. And, if President Reagan is successful, all indigents with TB will be treated under a medicaid program financed 100 percent by the Federal Government. What incentive will States then have to divert block-grant money away from such uses as rat control and hypertension screening, if the Federal Government will pick up the entire tab? To me, it seems likely that the failure to establish a separate categorical grant TB program now will mean higher, not lower Federal expenses later—regardless of whether the Federal Government picks up 60 or 100 percent of medicaid costs.

To protect our children form unnecessary threats to their lives, to save millions of Americans who already have TB from serious health risks, and to save the Federal Treasury money, I urge this subcommittee to reaffirm the action taken only last session by Congress and appropriate the full $9 million authorized for tuberculosis control.

Thank you, Mr. Chairman.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

STATEMENT OF EDWARD N. BRANDT, JR., ASSISTANT SECRETARY FOR HEALTH

ACCOMPANIED BY:

MARJORY MECKLENBURG, DIRECTOR, OFFICE OF ADOLESCENT PREGNANCY PROGRAMS

WILLIAM FOEGE, DIRECTOR, CENTERS FOR DISEASE CONTROL

ROBERT GRAHAM, ACTING ADMINISTRATOR, HEALTH RESOURCES ADMINISTRATION

WILFORD FORBUSH, DEPUTY ASSISTANT SECRETARY FOR HEALTH, OPERATIONS

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. Now, our next witness, from the Department of Health and Human Services, will be Dr. Edward N. Brandt, Jr., Assistant Secretary for Health.

INTRODUCTION OF ASSOCIATES

Dr. Brandt, we welcome you. And please introduce your colleagues for the record.

Dr. BRANDT. Thank you very much, Mr. Chairman.

Senator SCHMITT. If you will hold just 1 minute.

[A brief recess was taken.]

Senator SCHMITT. OK, gentlemen. Dr. Brandt, would you proceed and introduce your colleagues?

Dr. BRANDT. All right. Thank you very much, Mr. Chairman.

To my right, Mrs. Marjory Mecklenburg, Director of the Office of Adolescent Pregnancy Programs; and to her right, Mr. Wilford Forbush, Deputy Assistant Secretary for Health Operations; to my left, Dr. William Foege, Director of the Centers for Disease Control; and to his left, Dr. Robert Graham, the Acting Administrator of the Health Resources Administration.

Mr. Chairman, the Omnibus Budget Reconciliation Act of 1981 authorized several new programs to be administered by the Public Health Service. Today, I will address four.

One, adolescent family life projects; two, tuberculosis control; three, preventive medicine training; and four, special health professions initiatives, as well as emergency response capabilities.

Since the President's budget for fiscal year 1983 has not yet been submitted to Congress, I cannot discuss new budgetary recommendations at this time.

ADOLESCENT FAMILY LIFE PROGRAM

Let me first describe proposed activities under the recently enacted adolescent family life demonstration program.

This program exemplifies the commitment that this administration has for resolving the problems due to unintended adolescent pregnancies.

No one can deny that the statistics on teenagers who are sexually active, as well as those who actually bear children, are startling and serious. The number of teenagers who are sexually active increased by two-thirds during the 1970's. There were over 560,000 births to teenagers in 1979, and the rates for births to teenagers in the younger groups, under 15, are at some of the highest levels ever observed in the United States.

Moreover, the number of out-of-wedlock births to teenagers is close to a record high. The increase in such births to young women under 18 has been from 48,300 in 1960 to 105,600 in 1970 to 129,500 in 1979.

The risk of maternal death for adolescent mothers is higher when compared to women even in the 20- to 24-year-of-age bracket. The risk of complications of pregnancy and child birth, such as toxemia, anemia, and premature and prolonged labor is also higher.

Senator SCHMITT. Doctor, could I interrupt and ask you if you interpret in the figures you just gave us a lessening in the rate of growth of this problem?

Dr. BRANDT. It would appear that from 1970 to 1979 that there was a lessening in the rate of growth of the number of births, certainly in teenaged mothers.

If you look at the birth rate for women 15 to 19, the rate has tended to decrease somewhat, but not nearly at the rate that it has decreased for women at the age of 20 to 24. Their rate is down by about 50 percent in the past 20 years.

Maternal mortality, on the other hand, is also down in both of these age groups, but, again, it stays consistently higher for those under 20 as compared to those aged 20 to 24.

Senator SCHMITT. Are you talking about rate per thousand, something like that?

Dr. BRANDT. Yes; rate per thousand.

Senator SCHMITT. Rather than the absolute? Are the absolute numbers in those age groups going down?

Dr. BRANDT. The absolute numbers are going up, but at a slower rate than it was.

Senator SCHMITT. I mean the absolute numbers of teenagers in a particular age category of——

Dr. BRANDT. Is going down, yes.

Senator SCHMITT. Is going down, but the rate per thousand——

Dr. BRANDT. Yes; on a per thousand basis, both the birth rate and maternal mortality rate are going down. However, the rate of decline is higher for women aged 20 to 24 than for those under 20.

I would like to see programs aimed at the teenage pregnancy problem implemented in every State, and I believe that the block-grant funding to States can help promote such a development.

Furthermore, the Federal Government would continue to play a key role through the implementation of the adolescent family life legislation. The orientation of the Office of Adolescent Pregnancy Programs would be to develop and evaluate models of service delivery programs which could be utilized by the States and local communities. Specifically, the new authority would permit grants to: One, support the development and evaluation of different methods of service delivery for prevention projects to reach teenagers before they become sexually active; and two, promote research on contraceptive use, pregnancy and childbearing, and other aspects of adolescent sexual activity.

These grants would emphasize the participation of family members as an essential aspect in the comprehensive range of services to adolescents. I personally am hopeful that the role of parents and other family members, together with the other services and research components of this program, will be a positive intervention in reversing the high incidence of pregnancy among teenagers.

I turn now to tuberculosis control.

TUBERCULOSIS CONTROL

Authorized in the Omnibus Budget Reconciliation Act of 1981 was a new project grant to States for tuberculosis control programs. You can be assured that the administration shares the concern of Congress over the Nation's tuberculosis problem.

Furthermore, the preventive health and health services block grant is now in place. We believe this block grant offers a superior approach to prevention, including the control of tuberculosis, allowing States, therefore, to respond to problems such as this.

Since the beginning of the second quarter of fiscal 1982, 48 States and 5 of the 7 eligible U.S. territories have been implementing this block grant. The block-grant approach enables States to plan, coordinate, and target appropriate statewide services to meet the special needs of their population.

States are already familiar with this method of funding. Prior to the enactment of the preventive health block grant, the States were primarily responsible for disease prevention activities and received Federal funds under the health incentive formula grant program to assist in their efforts. One area supported by section 314(d) funds in the past has been the States' tuberculosis control programs.

Through the preventive health and health services block grant, States will continue to maintain their tuberculosis control activities. In fact, in those States which may see an increase in the incidence of tuberculosis, the block grant provides the flexibility to channel additional resources to the treatment and control of tuberculosis, thereby allowing States to tailor their preventive program to their own needs.

I would add that the Centers for Disease Control is a center of national expertise on tuberculosis, routinely gathering information on the incidence of this disease, providing expert information and techniques for tuberculosis control to public health agencies, and conducting studies on special disease problems.

TRAINING IN PREVENTIVE MEDICINE

Turning to training in preventive medicine, it is a new program which emphasizes specialized residency training in preventive medicine which was established in the Health Professions Education Act by the reconciliation bill. Grants and contracts are authorized for schools of medicine, osteopathy, and public health to support this type of training program.

Further, financial assistance would be offered to residents who plan to specialize or work in preventive medicine.

The President's proposed initiatives in health professions training are to improve the availability of well-trained health professionals in underserved areas, and to reduce health care costs through health promotion and disease prevention.

Five targeted areas of special national interest are the focus of the administration's initiatives. These include: Education and training of allied health personnel for health promotion and disease prevention; innovative projects to increase the production of and enhance the placement of podiatrists in underserved areas; provision of clinical training to health professions students in areas that are geographically remote from the primary teaching facilities and where medically underserved populations reside; continuing education to health professions personnel, especially those who provide primary care; and improvement and strengthening of curriculums in schools of veterinary medicine regarding care of food-and-fiber-producing animals.

EMERGENCY RESPONSE CAPABILITIES

Last, you have requested information on the Public Health Service's emergency response capabilities. As you know, the Public Health Service does assist States and other Federal agencies in emergency situations which pose an immediate threat to public health. The natural disaster at Mount St. Helens and the Three Mile Island incident are two recent examples of such public health threats.

The Public Health Service never had a separate emergency fund. We have successfully responded to public emergencies through the use of currently appropriated funds and the capability to reassign commissioned corps officers, which now number 6,000, as needed.

Such capabilities augment emergency response activities of other major Federal agencies such as the FEMA and the Department of Defense.

In addition, an expansion of emergency response capabilities has recently been included in the EPA superfund legislation.

That concludes my statement, Mr. Chairman. I would be happy to respond to any questions that you might have.

ADOLESCENT FAMILY LIFE DEMONSTRATIONS

Senator SCHMITT. Thank you, Doctor.

Does the Department have any reservations about attempting to solve the adolescent pregnancy problem through a Federal, categorical program of this kind rather than through encouraging efforts by the States under block grants?

Dr. BRANDT. Remember that the program that would be administered by the Department through the Office of Adolescent Pregnancy Programs is principally a demonstration program. We hope to demonstrate the ways in which the States can respond more effectively, and the ways in which the States can better organize and deliver their services.

This, I think, will be particularly appropriate when we deal with different population groups in different areas of States.

Mrs. Mecklenburg may have something to add to that.

Mrs. MECKLENBURG. I think that Dr. Brandt has represented exactly what we understand as the intent of the legislation. And you, yourself, Senator Schmitt explained it well when questioning Senator Denton; that we are, in fact, not sure what ways are the best ways to address the problems of prevention and support.

We do have some ideas that seem to be working in some areas of the country. It is our intention, under this legislation, to have an opportunity to look at model programs, to evaluate them carefully, and to disseminate the best ideas to the States so that they could then take the responsibility for this problem which does exist nationwide.

Senator SCHMITT. But you assume that the States cannot take the responsibility without such a program?

Mrs. MECKLENBURG. For instance, in the maternal and child health block or any of the other block grants, there are many competing priorities and programs, many worthwhile uses for the funds. Under these circumstances, it is very difficult to focus on a very special population, particularly in a way in which research and evaluation are emphasized.

It tends to be much more service-oriented, which is important, but only when one has facts about what kinds of services are cost effective, do we get the desired results and improvement in service delivery and client outcomes. We know, and we have heard from many people around the country, that there is a need to have more information and more models to choose from and more ideas before the States and service providers can effectively deal with the problem.

DISSEMINATION OF INFORMATION ON ADOLESCENT FAMILY LIFE DEMONSTRATIONS

Senator SCHMITT. What proportion of the resources that might be allocated for this will be used in a clearinghouse capacity so that that information does get around? There are a lot of experimental programs, I presume, even today privately funded, State-funded, university-based, school-based, and so forth.

Do you anticipate that a fair proportion of these funds will be used just for purposes of integration and for dissemination?

Mrs. MECKLENBURG. We are looking at, of course, the legislation, and until we know what the final appropriation is, we cannot determine what the proportion would be exactly. But information sharing is a very high priority.

We have already begun a number of ways of sharing that information in the present program. We have sponsored forums in which we have invited over 60 national groups to participate on an ongoing basis to share information and ideas; as we communicate with them, they can communicate with their members throughout the country, the ideas that we now have in place and the new initiatives that we plan.

I can't tell you the exact proportion of the money that will be spent, but I do think that I can guarantee you that we are very much aware that information sitting on the shelf or buried away in the bureaucracy is not going to help anyone in the country implement a program, and we are dedicated to finding cost-effective ways to get information into the hands of the people that need it in order to make decisions wisely.

Senator SCHMITT. But as yet, you haven't defined what those "cost-effective" ways are?

Mrs. MECKLENBURG. No; for instance, having access forums and capability to deal with organizations throughout the country and exchange information and utilize their channels of information is very cost effective. I mean, that costs almost nothing. That is one example. The extent to which we will print many booklets, distribute research studies, and the like, depends on the appropriation level. We do not have a specific amount of money set aside for that purpose. We are examining all the options and opportunities and the costs.

I would be happy to provide you with additional information about this.

Senator SCHMITT. As soon as the budget is available, of course, we would like to have a more detailed breakdown.

Mrs. MECKLENBURG. Right, but without a budget, it is difficult.

Senator SCHMITT. Would you anticipate there to be a register of projects that are funded under this program plus those projects that might have been funded had the program been in existence before this time so that a State like New Mexico or any other State could examine the register and have an abstract of the program and know who to contact to get more information without necessarily going through your office or any other form of bureaucracy?

Dr. BRANDT. I think we would have a register available, at least of the projects that are ongoing.

Certainly, our goal is to get this program out into the States. There is no question about that. Therefore, we will do whatever we can to assist the States in such programs.

I might point out that we are meeting fairly regularly with the Association of State and Territorial Health Officers on all of the block grants and all of the service programs to keep information flowing to them on a regular basis. This will inform them of successful projects, techniques that are being used, et cetera.

And certainly, we will do whatever needs to be done in order to make sure that the people around the country are clearly informed about how these demonstration projects are functioning.

PARENTAL CONSENT REQUIREMENT

Senator SCHMITT. One of the purposes of the adolescent family life program, as I understand it, is to "promote self-discipline and other prudent approaches to the problem of adolescent premarital sexual relations." At the same time, the proposed law requires that, except in certain limited cases, parental consent must first be obtained before any services can be provided to a teenager. Thus, a teenager could not obtain counseling under the program without the parents being notified.

Aren't these two provisions of the law in conflict?

Mrs. MECKLENBURG. We don't believe that the parental consent requirement will in fact discourage teenagers from coming to these service programs. In our view, the proposed service projects should not have any difficulty attracting teenagers.

For example, regarding pregnant adolescents, as the law states, approximately 80 percent of unmarried teenagers who carry their pregnancies to term live with their families before and during their pregnancy and remain with their families after the birth of the child. The families, indeed, are involved before, during the pregnancy, and after the birth.

ADOLESCENT PREGNANCY PREVENTION

Senator SCHMITT. On the prevention side, an 80-percent figure is meaningless; right?

Mrs. MECKLENBURG. This program, as you know, provides both prevention and support services. But the proposed projects, I think, could be very attractive to teenagers as a center for help and support. We find that when these centers are well run, what happens very often is that the teenagers who are enrolled in the program will talk to their peers, will talk to their siblings, and, in fact, the centers serve as a magnet to draw other teenagers into the program before they are pregnant and into the counseling sessions.

One of the possibilities under this program is to have pregnancy-care centers also involved more heavily in prevention. If you want to address the problem of prevention and parental consent as far as notification, it would seem to us that what we have seen in the literature is that most of the majority of teenagers already believe that their parents know that they are sexually active if they are coming to a family planning clinic or come to a place to get help; even though they think their parents know, they are not communicating with them.

I know there will be a great deal of sensitivity required in working with adolescents and with families so that a barrier will not be erected between them. But I also believe that parents are interested in their children.

Senator SCHMITT. I don't have any question of that. But I am just saying there is going to be a group—and we can argue over how large, what percent—that will not be able to take advantage of these services because they will not get parental consent; is that correct?

Dr. BRANDT. Possibly, but we don't know if it is 20 or 30 or 10 percent?

Mrs. MECKLENBURG. This is a demonstration program. We have to remember that the intent of the program is not to provide services to the population at large but to fund demonstration projects and research and evaluation projects. One of the things that we would hope to learn from these projects is what kind of a barrier, if any, exists.

And in no way does it represent, as a demonstration program, all of the other programs that might be available or all of the alternatives available to teenagers. There will be other programs in other parts of the country.

This, again, is a small demonstration program. We would be evaluating the kind of effect this approach does have. It is not the only approach. But we will find out if, indeed, it is effective.

APPROACHES TO PREVENTION

Senator SCHMITT. The authorizing legislation calls for efforts "to prevent adolescent sexual relations." What specific approaches would you expect grantees to use?

Mrs. MECKLENBURG. I think we have already covered a few of the kinds of things that might be available in the educational area. We have heard again from a number of people throughout the country already with their ideas and their projects even prior to funding or any notice of funds being available.

There is a multitude of educational programs possible, family-centered programs, programs of family life education. There would be the possibility of looking at the influences on young people within their peer groups, the effect of the media, the kinds of signals about sexual behavior and attitudes that are being sent to children, the kinds of messages they are getting, and the effect this has on their behavior. Are there alternative ways of providing other messages to them, and what kinds of results do they have?

We also hope to look at the correlation between other programs such as alcohol, drug abuse, suicide, and other problems that teenagers are facing in this country today. If kids are in crisis and some of the people working on these problems in a number of areas in this country have developed ways of identifying likely candidates for crisis and good ways of intervention, they have also found ways that didn't work.

And I would think that it would be very interesting as another idea to look at those kinds of other problems that adolescents are facing and to see if there is any interrelationship.

These are just a few of the kinds of ideas that have come to us already. I am sure there are many more.

Senator SCHMITT. I understand. And we are not here to change the law, but I do think you are going to run into problems of the inconsistency of requiring parental consent for services if the adolescent is not pregnant versus requiring such consent if the pregnancy has occurred. That is a tough set of criteria and difficult to administer.

RESEARCH ACTIVITIES IN ADOLESCENT HEALTH

On the research side, we have research in two other areas that I am aware of related to this. The National Institute of Child Health and Human Development has supported research in areas of adolescent sexual activity, pregnancy, and childbearing. Under its auspices, we have learned about the incidence of sexual activity and pregnancy among adolescents, about contraceptive use in this population, about the consequences of early childbearing, and a host of related topics.

In fiscal year 1981, NICHD funded 18 projects related to research on teenage pregnancy. How will this research under the active question today differ from research now being conducted by NICHD or authorized by the maternal and child health block grant?

Dr. Brandt. Research sponsored by the adolescent family life program will be directed research with a goal toward the delivery of services in an efficient manner. It will be operations research, if you will, as contrasted with——

Senator Schmitt. You would not expect to duplicate in any way——

Dr. Brandt. No, sir.

Senator Schmitt [continuing]. The ongoing——

Dr. Brandt [continuing]. No, sir. We have——

Senator Schmitt [continuing]. Statistical and health research, health-related research?

Dr. Brandt. That is correct. And as a matter of fact, we have formed an interagency coordinating committee to look at all of the research dealing with adolescents because we also have research at the National Center for Health Statistics where we collect family growth information on pregnancy and contraception for all age groups, including adolescents.

So it ideally will be to bring all this together and try to prevent duplication.

Senator Schmitt. Can we expect to see an objective evaluation of whether such duplication is going to occur and whether that research ought to be concentrated in one spot?

Dr. Brandt. If you would like us to provide an evaluation, we will certainly provide you with one.

Senator Schmitt. We now have four areas where this research is going on, if this is funded. You mentioned one; I mentioned two. I wouldn't be surprised, if we start looking around the Government, that we will find there are others.

Dr. Brandt. Yes.

Senator Schmitt. Because it has been a visible, and well-known problem, a serious problem. And I wouldn't even be surprised if in the National Institutes of Health, you will find some people are looking at the correlation of other problems with this broad-scale national difficulty of adolescent pregnancy.

ADOLESCENT PROGRAMS AIMED AT MALES

What about the male side of this issue? We tend to always talk about females. The male, as we all know, has some responsibility in this affair. Do you see any way to reach out to the male and try to inform him of the problems associated with adolescent pregnancy?

Mrs. MECKLENBURG. I think that is a good recommendation and one which——

Senator SCHMITT. It is not a recommendation; it is a question.

Mrs. MECKLENBURG. It has been done, and it is being done in some of the programs that we are funding now. And some of the programs which we will be looking at, obviously, that would be one of the components that we would hope to look at in a very targeted way.

There are programs that have a particular emphasis on finding ways to work with the male. And I think that that is a very important part of the problem, both in the prevention area and in the support area. And we definitely are looking for ways to encourage working with the male in present programs and in future programs.

Senator SCHMITT. Senator Abdnor, do you have any questions?

Senator ABDNOR. No, Mr. Chairman. Thank you.

Senator SCHMITT. Thank you. We will have some more questions for the record on that program.

Let's turn now to discussion of the tuberculosis program.

TUBERCULOSIS CONTROL PROGRAM

In response to questions asked by this subcommittee during the course of our fiscal year 1982 budget hearings, the Department of Health and Human Services indicated there seems to be an increase in reported cases of tuberculosis. The Department explained that although there has been a slow decline in TB for years, there are now indications that the direction of this trend may be changing.

From 1953 to 1978, the average annual decrease in TB cases was about 5 percent. In 1979, however, the overall decrease was only 3 percent. Data for 1980 show thus far that there was a 0.6-percent increase in reported tuberculosis cases. Data for 1981 showed an increase in the nature of 2 percent.

I am not sure those are statistically valid numbers. Maybe you can tell me in a few moments.

The incidence of tuberculosis in children is increasing at even greater rates. In 1979, there were nearly 1,000 new cases of TB reported in children which represents an 18.3-percent increase over 1978.

The Omnibus Reconciliation Act of 1981 authorized a new categorical grant authority for preventive health services for TB over a 3-year period: $9 million for fiscal year 1982, $10 million for fiscal year 1983, and $11 million for fiscal year 1984. No funds were requested by the administration specifically for this program in fiscal year 1982.

In addition to this new program, there are other new programs within the Department which may address the tuberculosis problem.

I would like to point out that we have Dr. Bill Foege, Director of the Centers for Disease Control, with us today. And I hope he can shed some light on these problems as we get into the questions.

TUBERCULOSIS AS A SERIOUS HEALTH PROBLEM

To what extent is tuberculosis now a serious health problem nationwide?

Dr. FOEGE. Mr. Chairman, I would list it as a serious health problem because we still have 27,000 or more cases of a disease that we have the technology to pretty well control. So it is a serious problem.

You are right. The declining incidence over the years has seemed to plateau for the last 2 or 3 years. And the 1981 and 1980 figures will be approximately the same. You understand, though, as part of that, approximately 8 percent of the cases last year were among refugees.

I say this because if there had been no refugee cases, we would have seen a substantial decline in the rate last year.

It is true that we are concerned about the ongoing transmission of tuberculosis quite aside from the cases coming into this country. This is best seen by the number of cases in children under the age of 5, and we have about 800 to 900 cases a year in children under the age of 5.

Senator SCHMITT. Is there any correlation in those cases with the areas with the highest refugee incidence?

Dr. FOEGE. Cases of tuberculosis among refugees have not shown much spread to the rest of the population. That is, the 2,000 plus cases last year in refugees were probably cases that were acquired before they came to this country. There has not been much transmission from the refugee population to the nonrefugee population.

INCIDENCE OF TUBERCULOSIS AMONG CHILDREN

Senator SCHMITT. Why is the incidence of tuberculosis among children still a problem?

Dr. FOEGE. The fact that we still have 800 or 900 children under the age of 5 as part of our endemic problem, quite aside from refugees, is evidence that we still have some difficulty in applying the information we already know about tuberculosis.

Senator SCHMITT. Are you saying that our ability to disseminate information has decreased and, therefore, you are seeing an increase in incidence among children?

Dr. FOEGE. No; it is a number of things. One, it is an area of missed opportunities; that we don't apply everything we already know, but we have problems developing.

For instance, the resistant strains, strains resistant to the commonly used drugs, have continued to be a problem, both primary and secondary resistance. We have now in the last few years had our first true outbreak, not simply cases, but true outbreak, of tuberculosis resistant to all three primary drugs.

But these kinds of problems have continued to plague us. Nonetheless——

Senator SCHMITT. Do you think that's why the problem with incidence of TB among children is continuing? I still haven't gotten an answer to that question.

Dr. FOEGE. I think we are seeing the problem in children simply because we don't apply everything we know. If we applied everything we know with every case of tuberculosis, we would go after all of the contacts, we would provide those who have positive skin test with prophylactic drugs, we would stop transmission. But we often get into this in the second generation.

Senator SCHMITT. Were we doing this a few years ago before this rise in children's TB came about?

Dr. FOEGE. Well, first, let me back up to say I am not sure there has been an increase in the rate.

Senator SCHMITT. I misunderstood you. I thought you said there had been.

Dr. FOEGE. No; we continue to have 800 to 900 cases a year in children under the age of 5 which shows there is ongoing transmission. But this is not an increase.

For instance, the rate in children, under the age of 5, 20 years ago was about 11 per 100,000. It is half that right now. So, we continue to see improvements in the tuberculosis problem.

The frustration we have is, it doesn't improve faster.

Senator SCHMITT. I understand. Is there any specific reason why we aren't applying everything we know? Is it a question of funding? Is it a question of the lack of State programs, or local programs?

Dr. FOEGE. I think one of the main reasons might be that as a country, we have assumed that the tuberculosis problem has gone away, and we have become a little bit apathetic. It is very similar to what happened with polio vaccine where after a very nice start in the 1960's, by 3 or 4 years ago, we were down to immunity rates of 60 to 65 percent in children.

So it was a matter of thinking the problem had gone away. I think that's where we are with tuberculosis.

PREVENTIVE HEALTH SERVICES BLOCK GRANT

Senator SCHMITT. To what extent are the States using the prevention block grant for TB control or planning to use it?

Dr. FOEGE. We can't be totally sure on that. The last year that we have good figures on would be 1980 when the section 314(d) money, the predecessor of the block grant, $6 million of that was actually labeled as being directly tuberculosis oriented. We think about $10 million, by the time one includes the laboratory services and so forth, is allocated to tuberculosis.

That is out of a total U.S. expenditure on tuberculosis of $150 to $200 million. So, something in the neighborhood of 5 to 7 percent came from the section 314(d) money. We would expect that States will continue to use the block grant now to supplement their own tuberculosis activities, but we don't have data on that.

SUSCEPTIBILITY TO TUBERCULOSIS

Senator SCHMITT. Does research show any genetic susceptibility to tuberculosis or is it purely an infectious disease?

Dr. FOEGE. It is a combination of environment, host, and the organism. There are groups of people that seem to have a higher susceptibility, but by and large——

Senator SCHMITT. In any environment?

Dr. FOEGE. In any environment.

And there also seem to be groups of people that are better transmitters. So that within a given environment, a person with some sort of genetic background may be exposed to people who are better transmitters. But it is also a disease of poverty. And we see this in crowded, low socioeconomic groups, particularly in urban areas of this country.

CATEGORICAL GRANTS FOR TB CONTROL

Senator SCHMITT. If the Congress decided to provide categorical funds for TB activities, do you think the funds could be used effectively relative to the block-grant approach?

Dr. FOEGE. I think that, given the fact that the Federal Government has only been involved in 5 to 7 percent of the total funding in the past, that can be made up by the block-grant approach. And I would think that, in answer to your question, if the money would be available, how would it be most effectively used or would it be used effectively?

Tuberculosis is not a uniform nationwide problem. There are some specific problems, particularly where there are refugee populations, where that sort of money would be used.

EDUCATION ON TUBERCULOSIS AND OTHER HEALTH PROBLEMS

Dr. BRANDT. I think, though, Mr. Chairman, it is important that one of the things that we have to do a better job of is making the American people aware of the fact that TB is a problem in this country. I think we have become very lackadaisical. Most people, in fact, don't recognize that tuberculosis still occurs and that we still run a risk.

We had last year roughly 27,400 cases of TB in this country. That is a sizable number. And I think we need to make people aware of the fact that it is still a disease that deserves attention.

Senator SCHMITT. Do you have any kind of public awareness communications program?

Dr. BRANDT. We do with the States. We communicate with the official State agencies. And most of them have some way of communicating with the public. Our activities in dealing directly with the public are somewhat limited.

I think we are going to have to make more people aware of the extent of this problem, particularly so that children will get treated early and so that we can identify people who may develop the disease.

Senator SCHMITT. Do you have resources to undertake a national program of communications?

Dr. BRANDT. We will do it along with our other prevention activities that are going on.

Senator SCHMITT. How many diseases would you say are in this complacency category? Polio, TB, what else?

Dr. BRANDT. Well, I think most of the diseases——

Senator SCHMITT. Can we be complacent about smallpox?

Dr. BRANDT. We can be complacent about smallpox at the present time, yes, sir.

Senator SCHMITT. Except for those cultures that are in the laboratory. You have to be sure they stay there; right?

Dr. BRANDT. Yes; Dr. Foege is very careful about keeping them there. But I think that we have become very complacent about many of the childhood diseases that were scourges a few years ago. It constantly requires alerting people. Now that all the States have mandatory immunization laws, it is less of a problem than it used to be, but you still will find children that are not immunized against diphtheria.

Senator SCHMITT. Will you make a special point to identify for us in your regular testimony later on in this budget cycle the resources you have to communicate this problem of complacency about diseases to the public as a whole, as well as to the public health agencies at the State and local level?

Dr. BRANDT. Yes; we will do that.

Senator SCHMITT. As you know, Secretary Schweiker, when he was in the Senate, and I have been traditionally very concerned about this. You don't have to be inattentive very long before suddenly you have a large, exposed population.

And it would be of interest to the subcommittee to know just what resources you have at your command or expect to have at your command in this budget cycle as well as later ones for this purpose.

Dr. BRANDT. All right, sir.

Senator SCHMITT. Senator Abdnor?

By the way, gentlemen, since both of you have come in a little bit late, we have five issues that are being discussed here today—the adolescent family life program, which we have more or less covered in questions, but certainly can return to; tuberculosis control; preventive medicine residency; special health professions initiatives; and emergency fund resources.

So, Senator Abdnor, if you have any urgency in your attendance here today, you can proceed on any of those subjects or anything else you care to talk about.

Senator ABDNOR. I'm sorry I was late. I'm here for a few minutes. It seems as though I come and go in a hurry.

IDENTIFICATION OF CASES OF TUBERCULOSIS

Regarding tuberculosis control, I have problems with prevention as well as identification. Do we have a good system for identifying cases, particularly in the schools to detect it early? Or are cases pretty well progressed by the time you encounter the disease? How does it work? Do you have any programs directed at identifying cases?

Dr. FOEGE. Yes; these are State programs, and we have shifted quite a ways over the past 20 years from where we used to go to schools and do skin tests on all the children and follow up those with positive skin tests to concentrate on known cases of tuberculosis and try to find their contacts.

It turns out the skin test positive rate in schoolchildren is now so low that one does not get much yield from going through schools. Less than 1 percent of children will have a positive skin test. So most of the attention is placed on, once you have identification, finding contacts and skin testing them.

But I think the diagnostic system in this country is really quite good.

Senator ABDNOR. Is that where the usual outbreaks occur, where there has been a case in a limited area of the school? That is where you are going to find the new ones or additional ones that crop up here and there and everywhere; right?

Dr. FOEGE. We have belts of tuberculosis in this country where one expects higher rates. In the southern part of the United States, in central city areas, in areas where refugees have concentrated, one tends to have tuberculosis.

In your State, there is relatively little tuberculosis. There were only 66 cases diagnosed all last year. So it is a disease that is not evenly spread across the country.

Senator ABDNOR. Years ago, my State had a good center for treatment. I am not even aware if we have one now. Do most States maintain institutions or facilities? How is it handled now?

Dr. FOEGE. One of the great changes that took place in the 1960's was to stop in-patient care for tuberculosis, by and large, and treat people on an out-patient basis. This could be done for several reasons.

Most cases were being found early so they were not so sick.

No. 2, it was found that with 12 to 15 months' treatment on an outpatient basis, people could be very quickly made noninfectious and could go back to work and continue a normal life.

So most of the treatment of tuberculosis today is done on an outpatient basis.

Senator ABDNOR. Who follows this—the State? Is it the State's responsibility when a case is discovered? Does the State follow up to see that the proper treatment and care is undertaken?

Dr. FOEGE. It is the State's responsibility. And oftentimes, the local health department does the actual followup. And the State monitors what is happening throughout the State.

Followup, as you can imagine, is one of the very tough parts of this entire problem to make sure people stay on their medication for a year's time.

TRANSMISSION OF TUBERCULOSIS

Senator ABDNOR. I shouldn't be taking the time, but what is the biggest contributor to tuberculosis? I mean, it is a disease. Is that the only way you can contact it? It isn't in the air or anything else?

Dr. FOEGE. It is a disease transmitted by a certain type bacterium, largely through respiratory spread. It ordinarily takes very close contact. It is not the sort of thing one gets from passing a case of tuberculosis on the street, by and large. Usually, it takes close household contact.

Every once and a while, one finds a transmitter who is so efficient that they can transmit it from many feet away, but by and large that doesn't happen.

People who are most susceptible are people who are malnourished, people living in suboptimal environment, or have a genetic tendency to tuberculosis.

Senator ABDNOR. Thank you.
Senator SCHMITT. Thank you, Senator.
Senator Burdick. Welcome.
Senator BURDICK. Thank you, Mr. Chairman.
Senator SCHMITT. Happy new year and all that.
Senator BURDICK. Same to you, and all that.

TRAINING IN GERIATRIC MEDICINE

Dr. Brandt, in the 1982 Appropriations Committee Report, curriculum development in geriatric medicine was one of the priority areas mentioned for fiscal 1983 funding. In the report, we requested that the Department report on their plans for development of this program at the fiscal 1983 hearings. I am concerned that your statement made no mention of this program.

Is the administration planning to implement this authorization? And if so, when can we expect to hear about your plans?

Dr. BRANDT. Of course, our approach to this has been principally to have schools implement geriatric educational programs along with the general primary care programs that they currently have underway. We are, in fact, working with them in the whole general area of primary care and preventive medicine, since geriatrics is not a recognized specialty. We hope to bring the appropriate knowledge that is needed to treat geriatric patients into those specialties. They are family physicians, internists, general surgeons, and psychiatrists.

I think those programs are in fact underway.

Dr. Graham may have something to add to that.

Dr. GRAHAM. Simply to say in addition to that strategy, Senator, we are also working with the programs of nurse practitioners and physician assistants, all in the primary care program area. We are trying to provide an emphasis through our granting mechanisms on the development of special competencies in geriatrics.

AREA HEALTH EDUCATION CENTERS

Senator BURDICK. The special initiatives program also got money for support services necessary to try to keep health professionals in shortage areas. We have already established such a program at the University of North Dakota, and it has wide support throughout the State.

It seems to me that this is just the kind of thing this program should support. Could one of you good doctors spend some time on that observation?

Dr. BRANDT. I presume you are talking about the Area Health Education Center, Senator, run by the University of North Dakota School of Medicine?

Senator BURDICK. That is correct. In those educational centers, available funding will support the same number as in 1981; isn't that correct?

Dr. GRAHAM. Yes; that is correct.

Dr. BRANDT. We will continue exactly as we have been doing in the past.

Dr. GRAHAM. I think it is also possible, Senator, that you are raising the question about the specific support services provision that was in the Omnibus Budget Reconciliation Act of 1981.

Because of the budgetary constraints, we did not in 1982 seek any appropriation for that nor was an appropriation forthcoming under the continuation resolution for that program.

Senator BURDICK. Is your answer addressing what we might do in fiscal 1983?

Dr. GRAHAM. I think it would probably be more appropriate to discuss this during the regular fiscal 1983 hearings after the President's proposed budget has been presented.

ELDERLY CARE

Senator BURDICK. When I chaired the hearing in Grand Forks, N. Dak., on related problems, there was strong support for home care for the elderly. Do you have any comments to make on the potential we have there to save money and also provide care?

Dr. GRAHAM. There is one area that we are working on within the Health Resources Administration that applies to this, and it might be appropriate for Dr. Brandt to comment on some of the other PHS and HCFA areas, but we are working specifically within the nurse practitioner programs to try to develop and provide a type of training which is appropriate for carrying nurses in nursing practice to participate in home/work programs.

That is one emphasis we are working with, and obviously the other is primary care, to the extent we are able to develop more primary care practitioners of all types. It is more likely those services will be provided in home settings rather than institutional settings.

Senator BURDICK. Thank you both, gentlemen.

Senator SCHMITT. Thank you, Senator.

PREVENTIVE MEDICINE SPECIALISTS

On the preventive medicine residencies issue, the Omnibus Budget Reconciliation Act of 1981, established in the Public Health Service Act a new authority of assistance to schools of medicine, osteopathy, and public health to develop or improve residency training programs in preventive medicine. Would you tell us more about this program and what may be needed?

Dr. BRANDT. Preventive medicine is a specialty which is concerned with programs at the community level which aim to prevent disease and to promote health. It is an established medical specialty with board certification, a defined curriculum, and has all of the other aspects required of a medical specialty. It has a 3-year residency. And there are, I believe, in the country at the present time about 360 or so residents in this area.

The goal of such residency programs is to train people so that they can influence community approaches to the control of disease and promotion of health. That is a quick overview of the specialty and the programs.

Senator SCHMITT. Could these programs deal with, principally, prevention of what they think of as common diseases, or do they deal with the elimination of bad habits which are the principal problem?

Dr. BRANDT. I think the basic orientation of the preventive medicine specialist is twofold: One is to initially make, if you will, a community diagnosis to determine the problems that exist in this community, and then to introduce intervention techniques.

Clearly, you are quite right in stating that the issue of changing one's lifestyle is one of the more difficult tasks that we face in this country. A doctor in preventive medicine is educated in these techniques within the limits of our current knowledge.

Trying to get people to change their behavior so as not to smoke, not to abuse alcohol, and to lose excess weight, is not a simple task. But it is one area where we are going to have to exert greater effort. People are responsible for their own state of health and must live up to that responsibility.

Preventive medicine people are trained to devise strategies that would accomplish those goals.

PREVENTIVE HEALTH STRATEGIES

Senator SCHMITT. Doctor, when one looks at the field of science, I don't think many would argue with the statement that we are truly into a bioscience revolution today in deciphering the human body. Four billion years of evolution has created what we are today in an extraordinary crucible of experimentation in which we are finding that the body has really figured out all its problems. Human life has developed mechanisms in many cases to deal with the problems that have been here for some time and those that we are creating for ourselves.

I think it is safe to say that we really have done no more than provide a drop in the bucket to develop an infrastructure for preventive medicine. How are we going to match that great potential that is developing at jet-plane speed within the basic science of genes and how they work or don't work—monoclonal antibodies, chemical defensive systems, a variety of opportunities to use the common DNA techniques to produce large amounts of natural human defensive chemicals and other substances?

How are we going to get the community as a whole to begin to reorganize itself so that, in fact, it can use this fantastic potential, take advantage of it, and start literally reducing health care costs because people aren't getting sick?

Dr. BRANDT. Let me just address the last statement you made first and say that I think the reduction in health care costs from a prevention program is a long-term one. We should not anticipate nor evaluate prevention efforts by cost saving on the short term.

There are a lot of us that are around who have already got problems that are going to show up.

Senator SCHMITT. Sewn the seeds of our own destruction.

Dr. BRANDT. We have already done that. And the reaping will come in the not too distant future. So the immediate cost savings to the public may not be that great.

On the other hand, one of the principal points that we must remember is that a healthy lifestyle, in fact, gives you a better quality of life, by preventing recurrent illness. The real reward is that you feel better, and you are able to do things. Your quality of life and your resultant happiness is, therefore, greatly enhanced. I think we have to emphasize that more and more.

Marshaling all of the forces that are there and attempting to bring them to bear on the issue of prevention is the principal activity of the Public Health Service. We are attempting to develop the plans and the approaches that will allow us to accomplish precisely what you are talking about.

Let me just give you a few ideas of the courses we are taking. We have established a new office in the Office of the Director of the NIH. The concern of that office is precisely to do two things.

One, to identify research that is taking place or has taken place at the NIH in recent years that is directly applicable to prevention.

Second, is to look at the impediments to the application of those results, again as it relates to prevention. That is not to exclude all of the ongoing research and development of monoclonal hybridomas for vaccine development and other kinds of areas.

We used to say "from the laboratory to the bedside." Now, we are really talking about going from the laboratory to the home or to the doctor's office.

We are working with the medical schools to implement the teaching of prevention throughout the curriculum instead of providing just a single course.

Having been a dean of a medical school, I think the one thing that medical educators have learned is that areas such as nutrition and prevention cut across all the disciplines. We must incorporate it throughout the entire curriculum. Pediatrics does a superb job of teaching preventive measures for children.

We have not been so successful with education in the treatment of adult problems, and particularly in attempting to introduce measures applicable to geriatric care. We are working with the medical schools, attempting to improve in this area.

The Public Health Service has defined a number of measurable objectives within 15 priority areas. These objectives, if achieved, would significantly improve health. We are attempting to identify at least three areas and by marshaling our resources and our knowledge we hope to see a reduction of morbidity and mortality.

We are also developing legitimate research, and we will in fact continue that research effort in a significant way. So I think we are developing a comprehensive prevention program. We are trying to accomplish what you are asking us to do. And I hope that in a year or less, I will be able to report to you some significant progress.

Senator SCHMITT. Do you sense the OMB recognizes the long-term potential of preventive medicine?

Dr. BRANDT. I think the OMB recognizes the long-term potential; yes, sir.

Senator SCHMITT. So, when we see the administration's fiscal 1983 budget, we can anticipate line items related directly or indirectly to our ability to prevent disease, curing it absolutely when it occurs, without recurring expensive treatment? That will have been protected, enhanced, through this fantastic process that we call the budget process?

Dr. BRANDT. I am not sure you will see it in line items, but I think in our testimony, we will, in fact, identify those activities; yes, sir.

Senator SCHMITT. Well, I will look forward to that. But I will tell you I haven't seen much recognition, within this or any other administration at the highest policy levels, of the role that science and technology generally plays in our future, much less that played in our past.

And I certainly will look forward to getting some encouragement from your future testimony.

Dr. BRANDT. All right, sir.

PREVENTIVE MEDICINE PROGRAMS IN MEDICAL SCHOOLS

Senator SCHMITT. How many schools actually have residency training programs in preventive medicine? Do you know?

Dr. GRAHAM. I believe the number of combined medical and public health schools right now is in the neighborhood of 30, but I may be able to pull that number out for you in just a second.

We can supply that for the record. We have it only in terms of aggregate residents right now.

[The information follows:]

PREVENTIVE MEDICINE RESIDENCIES

A total of 35 schools sponsor residency programs in preventive medicine—23 medical schools with 1 or more preventive medicine residencies programs and 12 public health schools. Based on information in the annual report: "Medical Education in the United States, 1980–81"—JAMA, 246: 2939, December 25, 1981, there are 77 accredited residency programs in preventive medicine in the United States.

IMPLEMENTATION OF PROGRAM

Senator SCHMITT. Do you expect them to respond significantly if this program is implemented?

Dr. GRAHAM. Yes, sir, we do. Traditionally, during the past 10 years, we have been able to provide a fair amount of support to residencies in preventive medicine, both medical and public health schools. Some of the changes in authorities over the last 4 to 5 years have changed that support. We really are proposing to support this as an area of high priority.

SPECIAL HEALTH PROFESSIONS INITIATIVES

Senator SCHMITT. In the area of special health professions initiatives, it is my understanding the administration's initial proposal with respect to these initiatives focused on keying the program into five or six specific areas. The Reconciliation Act authorized about 24 different initiatives under this program. Does this represent a significant change?

Dr. GRAHAM. Mr. Chairman, what happened last year is that the administration proposed essentially a replacement of the then section

788(d) with these five areas of priority. The outcome of the reconciliation action was essentially to retain the section 788(d) programs with some add-ons, but no money.

Senator SCHMITT. And the add-ons are what you are less excited about?

Dr. GRAHAM. Well, it is a matter in terms of our proposal of feeling that the five areas that we had identified before the Congress last year were in our judgment and within the budgetary limitations the areas of highest priority for special initiatives in health professions.

The additional four areas of priority that were identified in the reconciliation process in part overlapped in a couple of the areas that we were concerned with and in part did not overlap with our proposal.

One area of overlap was podiatric medicine. Another area of overlap we touched lightly on with Senator Burdick's question was the area of geriatrics.

Senator SCHMITT. The administration's proposal last year did not specifically call for "planning, establishing, and operating projects to provide support services to health professionals practicing in health manpower shortage areas," as outlined by the Reconciliation Act.

Do you expect to request money for projects providing support services to health professionals practicing in so-called health and manpower shortage areas?

Dr. GRAHAM. I think that is a fiscal 1983 question.

Senator SCHMITT. Well, it is, but will the administration request any funds at all?

Dr. GRAHAM. I think the response to your question should be in the context of the 1983 budget when it is presented.

Senator SCHMITT. I hope you realize that is an area of some interest to the subcommittee.

Dr. GRAHAM. I certainly do.

Dr. BRANDT. We are aware of it; yes, sir.

Senator SCHMITT. Do the existing authorities within the National Health Service allow an expansion of health professionals practicing in health manpower shortage areas?

Dr. BRANDT. Allow for expansion of that?

Senator SCHMITT. Yes.

Dr. BRANDT. Our approach to the National Health Service Corps has been to attempt to encourage private practice. One of the primary goals of the National Health Service Corps has been to convert health manpower shortage areas into nonhealth manpower shortage areas, if you will.

The issue is one of encouraging people to stay at a site or to remain at a site to avoid rotating a health professional every other year. We have put the emphasis now on the private practice option, permitting people to practice in health shortage areas at no cost to the Government. Not only have they fulfilled their obligation, but they are likely to stay in the area since they have lived there for some length of time and have set up and established a practice.

We think that the retention rate would be significantly higher.

With this option, we will be able to expand the number of National Health Service Corps members at no cost to the Government; they are earning their own keep and are meeting the needs of the people.

NATIONAL HEALTH SERVICE CORPS

Senator SCHMITT. One of the problems we have run into—and I appreciate the Secretary's cooperation on this—is that although contracts may run out for National Health Service Corps people, there may not be an immediate substitute for them. It is much appreciated that some accommodation to that situation has been worked out in several cases in New Mexico and I hope elsewhere. I welcome the Department's flexibility on this matter.

It is only commonsense that would seem to indicate while you are looking for somebody to fill in the slot that the person there, if he or she should choose to do so, should be allowed to continue their practice.

Dr. BRANDT. Certainly within budgetary and personnel limitations, we will attempt to do that. And we have been doing it pretty well this year.

Senator SCHMITT. I would assume there would be no significant budgetary limitations when it is a question of losing, say, the only professional in a significant area, and there hasn't been up to this point.

EMERGENCY RESPONSE

Under the Public Health Service Act, the Public Health Service has an ongoing responsibility to provide prompt and effective assistance to States and Federal agencies in emergency situations which pose an immediate threat to public health. If there is funding requested for fiscal year 1983 for the public health emergency response program, how would the fund function?

Dr. BRANDT. Such funds would be used to fund the cost of immediate response to emergency situations.

For example, in the Three Mile Island incident, the Public Health Service direct expenditure was $725,000. It is that kind of expenditure that would be reimbursed out of that fund.

Senator SCHMITT. What about State services? Are they reimbursed out of the fund in such a situation?

Dr. BRANDT. No; it was not our intention, at least, to do that.

Senator SCHMITT. These funds generally pay for what kind of activities—personnel or cleanup?

Dr. BRANDT. Yes; it is personnel, laboratory procedures, chemical testing, care of patients who may be exposed, care of people who may be exposed to various things, and so forth.

Senator SCHMITT. Is this the only way that such services can be provided or are there alternatives?

Dr. BRANDT. Generally speaking, the first line of response to a public health emergency is, of course, the State or within the State some higher authority. It is only when that problem exceeds the capacity of the State's resources to handle it that they would call upon us. We do not go into a public health emergency situation unless the State invites us with one exception. And that is an emergency involving a nuclear reactor where we do have certain authority.

Senator SCHMITT. Isn't that somewhat inconsistent, because the dangers posed to populations are much greater than certain other kinds of health emergencies? And we have already seen nuclear accidents——

Dr. BRANDT. Yes, sir.

Senator SCHMITT [continuing]. Chlorine tankcars, a variety of toxic chemical transportation situations. And you have to be asked before you can assist?

Dr. BRANDT. Yes; generally speaking, most States have greater ability to deal with those kinds of problems than we do.

PHS TESTING CAPABILITIES

Senator SCHMITT. What about your testing capabilities? One of my other hats is the Commerce Committee. And they were very interested in toxic materials testing capability. Do you feel that the Service is capable of moving in on request and determining the nature of the threat?

Dr. BRANDT. We have two possibilities. Actually, first, we have organized our toxicology for chemical testing, the toxicology program, into what is now known as the national toxicology program, which includes facilities at CDC, it includes the FDA's toxicology facilities which are in Pine Bluff, Ark., and then includes the facilities at Research Triangle, North Carolina, as part of the National Institute of Environmental Health Sciences.

By coordinating all of these laboratories, we can provide a pretty fair response to those emergencies. We also have the ability to contract with private laboratories or other Federal laboratories. Clearly not all of these programs involve short-term testing. Some of them take some time.

Senator SCHMITT. Describe your field testing capabilities.

Dr. BRANDT. Generally, we would prefer to collect the specimens and send them to a laboratory to allow more precise evaluation.

Senator SCHMITT. In some developing situations, you may not have that kind of luxury.

Dr. BRANDT. That's true. But I think we would attempt to make sure that the results are accurate first. And if it can be done accurately in the field, we would do it in the field. But each particular circumstance would dictate whether we would use our own equipment, or whether we would try to contract with somebody there on site, or whether we use facilities that are on site already such as in a local hospital.

Senator SCHMITT. There have been some interesting technological developments in the ability to monitor and predict the airborne spread of toxic substances and health hazards of other kinds. Has the Public Health Service looked at some of those new techniques or the rapid deployment of sensors or wind measurement devices in order to rapidly develop an analysis and printout of what the airborne danger is in a short period of time?

Dr. BRANDT. Let me defer to Dr. Foege and see if he can answer your question.

Dr. FOEGE. We are indeed looking at those possibilities. In fact, we have had some very nice demonstrations by the Los Alamos Lab of what capabilities they have in this area. So we are aware of what the state of the art is.

Senator SCHMITT. Let me also suggest that you talk to NASA and look at what they developed in order to monitor the potential spills of hydrozine and nitrous oxide from the Space Shuttle after landing. It was demonstrated at the Nashville Technology Showcase a few months ago. It is one that appears to be quite portable. And I suspect the sensor elements could be quite portable also.

You get a very rapid graphical display of what the distribution patterns and concentrations as a function of time are going to be in that way.

Dr. FOEGE. I will certainly look at that.

PRIMARY CARE RESEARCH AND DEVELOPMENT

Senator SCHMITT. Dr. Brandt, we have another topic where the subcommittee is most concerned about an authorizing problem involving primary care research and development projects. I refer you to a copy of a letter from both the House and Senate authorizing committees, pointing out a "technical error" in the program as reauthorized by the Reconciliation Act of 1981.

According to the letter, the authorizing committees inadvertently provided for funding primary care research and development projects only in urban areas of which there are only a few—perhaps only one.

Dr. BRANDT. Yes; only one.

Senator SCHMITT. The language apparently did not provide for funding projects in rural areas of which there are many. Obviously, this was within the intent of the law.

The joint letter from the authorizing committees states they intend to propose technical amendments to correct this omission and that the Department "if appropriate, make continuation grants to rural projects prior to the enactment of the technical amendments by Congress."

What do you intend to do to make certain the continuation projects in rural areas are funded to completion?

Dr. BRANDT. At the present time, we are hopeful that the Congress will, in fact, correct that error which would thereby give us the legal authority, the legal authorization, to fund those projects.

I think we are caught in that kind of a box right at the moment. I guess that some alternative may have to be developed. But at the present time, we are awaiting congressional action to correct that problem.

Senator SCHMITT. You don't feel you have any options?

Dr. BRANDT. We don't see that we have an option at the moment.

Senator SCHMITT. Have you responded in that vein to the authorizing committees?

Dr. BRANDT. It is my understanding that the Secretary has not yet responded to the authorizing committees.

Senator SCHMITT. When will we expect it to be?

Dr. BRANDT. I would hope that he will respond soon.

Senator SCHMITT. There are no reprograming authorities that you might have at this time?

Dr. BRANDT. It is my understanding we do not have reprograming authority to allow us to do this without authorization.

Senator SCHMITT. Unless this is resolved, I assume there would be no attempt to reprogram moneys intended for this program in other areas?

Dr. BRANDT. Well, I don't know whether there will be an attempt or not, but I would think that it would be unlikely.

Senator SCHMITT. I think it is safe to say that there would probably be no approval of a reprograming request dealing with these moneys if they were going to be used for a purpose other than funding primary care research and development projects in rural areas. Unless it is absolutely clear Congress is not going to act.

The Appropriations Committee certainly intended those moneys to be spent in the rural primary care area, whatever the law may say.

We will have to see if we can fix that other problem.

Dr. BRANDT. Yes.

Senator SCHMITT. In fact, it might be necessary to try to fix it on a supplemental bill that is going through right now.

To what extent is it true that projects whose present funding grant carries them into the third and fourth quarter of the current fiscal year would not immediately be threatened by this particular legislative problem?

Dr. BRANDT. I really can't answer that question, Senator.

I will ask Mr. Forbush.

Mr. FORBUSH. I am sorry, I didn't understand the question.

Senator SCHMITT. We have some ongoing projects whose present funding grant would provide funds through the third or fourth quarter of the current fiscal year. Are they threatened in anyway by this legislative quirk?

Mr. FORBUSH. It is my understanding that no project will be due for renewal until June.

Senator SCHMITT. That answers that question.

Well, ladies and gentlemen, I will let you go. I want to thank you for coming up here today to deal with these odds and ends of new health programs. Your testimony is going to be most helpful as we decide on the funding of these particular programs.

SUBMITTED QUESTIONS

We will have some more questions for the record. I hope we can have them answered promptly. Please provide the responses to us with the corrected manuscript.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

PARENTAL CONSENT REQUIREMENT

Question: To what extent is it possible that adolescents who cannot communicate with their families but who need counseling the most may be frozen out by the parental consent requirement in the law?

Answer: The preliminary stage of contact between the non-pregnant adolescent client and services staff should allow the opportunity not only to advise the adolescent about parental notification and consent procedures, but to discuss and perhaps dissolve barriers that are keeping the adolescent from opening up communication channels with his/her parents. We expect very few adolescents have family communication problems so severe that they could not tolerate parental awareness of their interest in prevention services. When possible, the adolescents who are deterred from seeking these services would be targeted for research attention in order to learn more about the dynamics of this kind of problem.

Question: Why is your policy inconsistent - requiring parental consent for services if the adolescent is not pregnant, but not requiring such consent if pregnancy has occurred?

Answer: Section 2006 (22) states that notification of and consent by parents or guardians is required for any unemancipated minor requesting services, with certain exceptions and provisos. The exceptions are noted in (B) which concerns testing solely for pregnancy or venereal disease, incest involving a parent, or certification by a blood relative that notification would result in bodily harm to the minor and (C) which involves those situations in which the minor would be compelled to have an abortion, (A) (ii) adds a timeliness dimension for pregnant unemancipated minors, requiring that the parents or guardians of such a minor be notified "within a reasonable period of time."

PREVENTION SERVICES

Question: If prevention services are defined as "services to prevent adolescent sexual relations," what mechanisms would be devised to determine which adolescents are eligible for these services?

Answer: The law defines prevention services as "services to prevent adolescent sexual relations," but it does not specify that such prevention efforts are to be directed to any particular subcategory of teenagers. All teenagers desiring to receive prevention services that will be made available in demonstration project form are eligible to do so, subject to all other requirements of the law. Therefore, there would not be a need to devise an eligibility mechanism to determine which adolescents are eligible for these services.

Question: How will grantees justify to their clients that nonpregnant adolescents are not eligible to receive family planning services and mental health counseling? Why, on the other hand, are pregnant teenagers or teenage parents then eligible to receive family planning services under this program?

Answer: Grantees will make every effort to assure that non-pregnant adolescents needing these services will obtain them. Our understanding of the intent of the Congress in defining eligible persons and the uses of grants in Sections 2002 and 2004 derives from the following: "Grantees may only provide contraceptive services using funds under this bill if (1) there are no other facilities for doing so in the community; and (2) if there are no funds available to the program from any other public or private source that could pay for such services. In the committee's view, money spent on birth control services under this program would divert resources from the purposes of the Act. The widespread availability of government subsidized birth control services should allow the adolescent family life program greater freedom to concentrate its efforts on discouraging premarital sexual relations and serving pregnant adolescents. Grantees are permitted to counsel adolescents about the availability of birth control services in the community." (Committee Report, July 21, 1981, p. 13.) The care services to pregnant teenagers which the preceeding Committee Report statement targets for concentrated effort traditionally have been comprehensive and inclusive of family planning services. One of the purposes of the Adolescent Family Life law is to establish innovative, comprehensive, and integrated approaches to the delivery of care services for adolescents.

RESEARCH

Question: What arrangements will there be to ensure that any research supported by the Adolescent Family Life Program would not duplicate other federally-supported research?

Answer: Several mechanisms exists within the Department of Health and Human Services to address the concern about possible duplication of research related to adolescent pregnancy. For example, an Interagency Coordinating Committee under the direction of the Office of Adolescent Pregnancy Programs (OAPP) exists to coordinate the research efforts of Title XX with those of other Federal agencies. In addition to such formal coordinating mechanisms, there has been an ongoing exchange of information and ideas between researchers at OAPP and the National Institute of Child Health and Human Development toward the end of avoiding duplication of effort as research plans for the Adolescent Family Life Program go forward. These and other existing processes within the Public Health Service assure that wasteful duplication will be prevented.

DEMONSTRATION BENEFITS

Question: What justification exists for funding yet another program addressing reproductive health-related needs?

Answer: The Adolescent Family Life Program is not a services delivery program. Its emphasis is on conducting research and evaluating demonstration services projects for the purpose of identifying models to be used by State and local deliverers of services. The care services to be demonstrated and evaluated by the Program are broader and more comprehensive than the medically-oriented services provided under the Family Planning Progam, Medicaid, and the Maternal and Child Health Program. The comprehensive service approach to teenage pregnancy care addresses the need for continuing education, job counseling, parenting education, etc., on the part of pregnant teens and teen parents, as well as the need for reproductive health-related care.

Question: How would the Department ensure there is no duplication between this program and services already being offered?

Answer: The Adolescent Family Life law contains a strong coordination requirement which will prevent duplication and overlap with other programs not only at the Federal level but at State and local levels as well. It requires grantees who receive funds for demonstration projects to report periodically to the Secretary concerning Federal, State and local policies and programs that interfere with the delivery and coordination of pregnancy prevention and care services. It calls for the review of all related programs administered by the Department and consultation with other Federal departments and agencies administering programs that could tie in with the goals of the Adolescent Family Life Program.

Question: If funding is provided for the Adolescent Family Life Program, how many grantees of the former Adolescent Pregnancy Program will receive funding under the new program?

Answer: It is difficult to state how many of the former Adolescent Pregnancy Program grantees will receive funds under the new Adolescent Family Life Program. While grantees will meet the grant recipient eligibility criteria, all will have to compete for the available funds. It should be pointed out, however, that these grantees have experience in the care area, and that they have been assisted by the Office of Adolescent Pregnancy Programs during the past year to start efforts in the evaluation area. Thus, these grantees should have at least equal footing to compete with other applicants who seek funding under the new legislation.

Question: How do you see the connection between the Adolescent Family Life Program and the Adolescent Pregnancy Program, which has now been placed in the Maternal and Child Health Block grant?

Answer: The Adolescent Family Life Program differs from the Adolescent Pregnancy Program in a number of important ways:

- The Adolescent Family Life Program concentrates on the development of models that will offer States and localities solutions that best meet their needs. In the area of service delivery, it will evaluate a number of approaches to find the most cost-effective and innovative methods of meeting the needs of pregnant adolescents, adolescent parents, their children and families.

- The Adolescent Pregnancy Program did not provide any funds for research activities. The Adolescent Family Life Program emphasizes research and will concentrate on investigating the causes and consequences of adolescent premarital sexual relations, contraceptive use, pregnancy and childbearing.

The complementary nature of the care services delivery efforts of the old Adolescent Pregnancy Program (retained in block grant form) and the demonstration services evaluation-research thrust of the new Adolescent Family Life Program should be evident: information gained from the latter will contribute to the effectiveness of the former.

GENERAL FUNDING

Question: If funds are not specifically appropriated for this legislation, can the Secretary of Health and Human Services still fund this program through the Departmental budget and, if so,

-- Specifically, where would the money come from?

-- How much money would be shifted to the Adolescent Family Life Program and in which areas?

Answer: Funding for the Adolescent Family Life Program is completely dependent on receiving an appropriation. If funds are not appropriated, the Secretary of Health and Human Services will not be able to fund this program through the Departmental budget.

Question: I know you don't want to talk about the forthcoming Budget, but if you ask for a FY 1982 supplemental won't that be inconsistent with your opening statement that block grant funding to states can help promote the development of programs in every State aimed at the teenage pregnancy problem?

Answer: The question appears to refer to the following opening statement by Dr. Brandt: "I would like to see programs aimed at the teenage pregnancy problem implemented in every State, and I believe that the block grant funding to States can help promote such a development."

Dr. Brandt also explained that the Federal Government would continue to play a key role through the implementation of the Adolescent Family Life legislation. A new Federal role will be to conduct research and evaluation activities in connection with demonstration services projects, so that model service delivery programs (in both the prevention and care areas) can be identified for dissemination to the State and community levels. The purpose of the Office of Adolescent Pregnancy Programs would be to develop and evaluate models of service delivery programs which could be utilized by the States and local communities. The request for a FY 82 supplemental to implement the Adolescent Family Life legislation at the Federal level is not inconsistent with States making use of block grant funds to provide teen pregnancy services, simply because the two levels of government will be performing very different functions in attempting to ameliorate the problem of teenage pregnancy. As a result, we would like to see programs in all 50 States, using approaches which have proven to be effective.

PARENTAL CONSENT

Question: We can all agree that it is desirable for young people to consult with their parents about any health care services they are seeking. I am somewhat concerned, however, that the parental consent and notification provisions in this legislation will impede the ability of physicians and other service providers to exercise their best judgment in deciding, with their young patients, when it is appropriate to involve the parents. Certainly, the parental consent provisions are far more restrictive than state laws, applicable court decisions and current professional practices. What assurances can you give us that minors will not be deterred from seeking services they need because they fear a loss of confidentiality?

Answer: The concern raised by this question appears to be based on the assumption that the purpose of the Adolescent Family Life Program is to deliver categorical services to a total population of adolescents. To the contrary, as the Committee Report (July 21, 1981, p. 15) points out, the Adolescent Family Life Program is "a Federal demonstration project and not a far-ranging Government entitlement program." The Committee Report further states that parental notification and consent requirements are for the opportunity to explore family-centered approaches to the problem of adolescent sexual relations and adolescent pregnancy. The Report views the requirements as "an attempt to determine the effect that parental involvement requirements might have on a small scale." (p. 15)

ABORTION REFERRAL

Question: Virtually every reputable health or social service agency provides counseling and referral for any service it does not itself provide, in accordance with generally accepted professional standards. Yet, under this legislation, any agency which provides counseling or referral for abortion, or which subcontracts with any agency which does so, is ineligible for a grant. It would seem to me that precludes virtually every established group, with the possible exception of "right to life" groups, from eligibility. Is my understanding correct?

Answer: The legal interpretation of Section 2011(a) is unclear and the Department's General Counsel is presently reviewing that section and the legislative history. We will provide the Subcommittee with further information on this matter once we receive the General Counsel's interpretation.

Question: You are familiar, I am sure, with the doctrine of "informed consent" which requires that individuals be provided with information about all medical options available to them and the risks and benefits of each before they agree to any course of treatment. Given the restrictions on counseling and referral for abortion in this legislation, won't pregnant adolescents be denied the information they need to make free and informed decisions about whether to proceed with their pregnancy? Follow-up question: If we require service providers to withhold information about one medical option--abortion--aren't we laying them open to malpractice suits brought by people who were only made aware of the option of abortion when it was too late?

Answer: As I said in reply to the previous question, the Department's General Counsel is reviewing Section 2011(a) and we will provide the Subcommittee with further information once we receive the General Counsel's intrepretation.

RESEARCH

Question: For over a decade, the National Institute of Child Health and Human Development has supported research in the areas of adolescent sexual activity, pregnancy and childbearing. Under its auspices, we have learned about the incidence of sexual activity and pregnancy among adolescents, about contraceptive use in this population, about the consequences of early childbearing and a host of related topics. Why do we need research conducted under different auspices in this field? Follow-up question: Will the research be subject to the same peer-view standards which apply for NICHD-sponsored research?

Answer: The research proposed under the new legislation has a different orientation from the adolescent pregnancy research efforts of the National Institute of Child Health and Human Development (NICHD), in that it is policy directed research and operations research that has direct application to the policies, services, and approaches needed to deal with the problem of adolescent pregnancy. The Adolescent Family Life Program will not duplicate the research efforts of NICHD, but will use them to the extent that they are applicable, and structure its research effort to take advantage of the unique opportunity of the Adolescent Family Life Program under which the Congress has brought together research, model demonstration projects, and evaluation in a single strategy under a single office. The Adolescent Family Life Law requires the Secretary to establish a system for reviewing research grants and contracts that is "substantially similar to the system for scientific peer review of the National Institutes of Health" (Section 2008).

TITLE X INFORMATION AND EDUCATIONAL MATERIALS

Question: Recently, an advertisement has been run on TV, produced by the Bureau of Community Health Services on money taken from Title X funds. The gist of this ad is that it urges girls to "Say No" to their boyfriends.

When was this ad campaign started and how much did the "Say No" campaign cost to produce and run?

Answer: "Saying No" is one of four television public service announcements produced to promote parent-child communication. The objective of the campaign is to urge parents to communicate information and values about sexuality to their children. The four spots were produced under a $100,474 contract awarded September 15, 1980. The spots were distributed individually at four to six week intervals between May and September 1981. The cost of distribution and placement evaluation was $9,996. While this spot is targeted at teenage girls, the other three spots, "Teachers," Messages," and "Waiting Room" are targeted at parents. Three of the four spots including "Saying No," have won media awards as public service announcements.

Question: What is the audience size this ad reaches?

Answer: During the 60-day period following release of "Saying No," it was reported as being telecast 4,409 times with an estimated viewing audience of 157 million. The spot is still being shown nationally. Estimates are made by Modern Talking Picture Service, Inc., a company which prepares such estimates for commercial advertisers.

Question: What has been the viewer response thus far?

Answer: There has been no formal evaluation of viewer response. Communications from parents, teens, educators and health professionals have applauded the Department for producing this spot and the campaign in general.

Question: How many have written in requesting further information?

Answer: A total of 526 copies of "Many Teens are Saying No" have been sent by the National Clearinghouse for Family Planning Information in response to write-in's from this spot. We know that some family planning agencies added a local tagline to the spots to enable viewers to receive information from community resources. We do not have any figures on response directed to local agencies. About 5,000 copies of the "Changes and Choices" booklet series have been sent in response to write-in's from the other three spots.

Question: Are there any current ads, or plans for one, which encourage a boy not to ask?

Answer: There currently are no ads targeted at the boy. A 17-minute film targeted at boys was released during 1980 and is available on a free-loan basis to schools and other community agencies.

Question: Please supply us with a copy of the material you send out to those who write in.

Answer: Copies of the storyboards for the four television public service announcements and the booklet series which are sent in response to write-in's from the announcements are being submitted for the Committee's files.

TUBERCULOSIS CONTROL

Question: To what do you attribute the decline in cases of tuberculosis through the late 1970's?

Answer: The decline in cases is attributable to a combination of the application of proven tuberculosis control measures by health departments, and the improved standard of living in the United States during the 20th Century. During the first half of this century, control measures consisted of mass casefinding programs, isolation of cases, and contact examination. Antituberculosis drugs were introduced about three decades ago. Health departments have since emphasized prompt identification and treatment of cases to interrupt transmission of tuberculosis organisms to uninfected individuals. They have also emphasized preventive drug treatment of contacts and other infected individuals to prevent their developing transmissible tuberculosis. These services are now almost universally provided on an outpatient basis, relying on health department personnel to ensure that patients adhere to therapy schedules.

Question: What difficulties do you foresee in bringing tuberculosis under control again?

Answer: The control of tuberculosis is not beyond reach. High quality care for tuberculosis patients is available in all areas of the Nation. Virtually all health departments conduct public health tuberculosis control programs.

The nature of the disease itself strongly favors the persistence of tuberculosis as a public health problem. While most infectious diseases produce clinical illness shortly after exposure, a person exposed to tuberculosis may develop the disease at any time--even decades later. A person carrying tuberculosis bacteria in the body has a lifelong risk of developing the disease. It is estimated that over 10 million people in the United States are now infected with tuberculosis bacteria. Large numbers of these infected persons are concentrated in certain population groups such as inner city residents, Native Americans, other ethnic minorities, the elderly, and the poor.

Also contributing to the persistence of this public health problem are immigrants, refugees, and undocumented entrants, many of whom have come from parts of the world where tuberculosis incidence and the risk of infection with tuberculosis bacteria are several times higher than in the United States. Many who are infected will develop tuberculosis, sooner or later, after entry into the United States. Although the vast majority of cases in the United States will continue to occur in persons born in this country, changing immigration patterns will play a part in defining the Nation's future tuberculosis problems.

TUBERCULOSIS IN REFUGEES

Question: How successful are refugee health efforts relating to tuberculosis?

Answer: The overseas screening program identifies refugees with infectious tuberculosis so that treatment can be initiated. On arrival in the United States, refugees under treatment and others with suspected (noninfectious) tuberculosis are referred to health departments for appropriate management by local health officials. The screening, referral, and notification system is functioning effectively.

In this country, refugees are treated for disease or infection like any other person in the United States. The quality of such individual treatment and care is generally excellent, but the ability of health departments to perform associated public health actions (e.g. contact followup, keeping difficult patients on medication) varies from community to community.

About one half of Indochinese refugees have evidence of subclinical, dormant infection. These individuals are not capable of transmitting infection unless they develop clinically active tuberculosis with symptoms, but they do have a small, lifelong risk that tuberculosis may develop. Many health departments are screening refugees for tuberculous infection and providing preventive therapy to reduce the risk of future tuberculosis disease. A number of health departments use Federal grant funds available through the Health Program for Refugees to help defray the costs of screening and initial followup.

Question: How can we do a better job to prevent or treat more effectively tuberculosis in refugees and other recent immigrants?

Answer: The impact of refugees and immigrants on the tuberculosis problem varies from State to State and from community to community. Communities with special tuberculosis problems do need to supplement tuberculosis medical care of high quality with effective public health prevention, control, and outreach activities. Many local health departments are using funds from the Health Program for Refugees to screen refugees for tuberculosis infection and disease, along with other health problems. Those communities which identify problems can also use Preventive Health and Health Services Block Grant funds to supplement State and local resources used for public health.

High quality diagnosis and treatment for tuberculosis are available in virtually all U.S. communities. With the exception of infectious cases who must be started on treatment abroad, it is desirable to get Indochinese refugees with suspected tuberculosis out of Southeast Asia and into the American health care system as quickly as possible so that complete, accurate diagnostic tests, drug susceptibility tests, and excellent treatment can be provided with confidence.

HHS TUBERCULOSIS ACTIVITIES

Question: The newly enacted Preventive Health and Health Services Block Grant may be used by the States for tuberculosis control activities. Within the Department of Health and Human Services what other programs now in existence directly address the tuberculosis problem? Approximately how much will be spent in FY 1982, in total, for tuberculosis activities in these programs?

Answer: There are several programs conducted within the Department of Health and Human Services which fund tuberculosis control efforts. The Health Program for Refugees provides Federal funds to local health departments which can be used to cover costs associated with screening and follow-up services for refugees. In addition, individuals are eligible to receive assistance under Medicaid; however, each State determines which services will be provided under Medicaid or any other state sponsored program.

The Public Health Service provides tuberculosis patient care as part of the overall health care program in the Indian Health Service and the Federal prisons. In addition, an estimated $4,138,000 will be spent in FY 1982 for NIH research grants, FDA investigation and approval of use and marketing of anti-tuberculosis drugs, and for CDC assistance to States including national surveillance, consultation, training and operational research.

Question: One purpose of this hearing is to consider the possibility of funding the new tuberculosis program regardless of whether or not there will be Administration requests either for fiscal 1982 or fiscal 1983. In your professional judgment, what level of funding is needed to help reverse the unexpected rise in tuberculosis cases in the U.S.?

Answer: There has not really been a rise in tuberculosis morbidity (except for a very small increase in 1980), but rather a leveling off of the long-term downward trend in reported cases. Provisional data for 1981 indicates a renewed decrease in the number of reported cases. Some areas experiencing morbidity increases or other special tuberculosis problems (e.g., drug resistance, disease in young children) may need to supplement existing resources allocated to such tuberculosis control activities as case reporting, outreach, evaluation, or prevention actions. These problems and needs vary from area to area and from year to year. Local factors determine the level of funds that are needed to meet local needs. The Preventive Health and Health Services Block Grant provides States with a flexible mechanism for augmenting State and local funding in response to changing disease patterns and temporary problems.

DRUG RESISTANT TUBERCULOSIS

Question: In our FY 1982 budget hearings, the Department also mentioned the problem of treatment-resistant tuberculosis bacteria. What is being done to deal with the problem of resistance to antituberculosis drugs? How serious is this problem?

Answer: The Centers for Disease Control (CDC) provides information on control and treatment of patients with drug resistant disease to State and local tuberculosis control programs through its Morbidity and Mortality Weekly Report, publication of scientific articles, presentations at medical meetings, and its training programs. Direct consultation with CDC staff is available to health care providers treating patients with drug resistant disease. CDC also trains laboratory personnel in the proper methods of performing drug susceptibility tests.

Since 1975, CDC has monitored resistance to antituberculous drugs among patients with previously untreated tuberculosis throughout the United States. This ongoing surveillance program provides data on changes in drug resistance patterns in different geographic areas and among different population groups. Special surveys of drug resistance among Indochinese refugees and Haitian entrants have also been conducted. Treatment policies have been revised based on these surveillance data in order to combat the problem of drug resistance.

Several CDC research programs are concerned with drug resistant tuberculosis. Among these are studies on rapid determination of drug susceptibility (currently used methods commonly require several weeks), studies on the epidemiology of drug resistant disease, and analyses of the most cost-effective methods of managing contacts of patients with drug resistant disease.

Data from the CDC drug resistance survey indicate that approximately 7 percent of United States patients with previously untreated tuberculosis have organisms resistant to one or more antituberculosis drugs and that this rate has remained relatively stable during the past 6 years. However, there are areas of the country with higher rates (approximately 15 percent). Most of these areas have large numbers of residents who were born in parts of the world where tuberculosis is very prevalent and drug resistance is common (e.g., Southeast Asia and Latin America). Approximately one-third of Indochinese refugees and Haitian entrants with infectious tuberculosis are estimated to be excreting drug resistant organisms.

Although precise data are not presently available, a substantial proportion of previously treated tuberculosis patients whose disease has relapsed have drug resistant disease. This most commonly occurs because of improper use of drugs or poor patient compliance with therapy.

Drug resistant disease is a potential threat to the effective control of tuberculosis. However, with proper use of available antituberculosis drugs and improved patient compliance, drug resistance should become less of a problem. CDC efforts in this area are helping to assure that eventuality.

FEDERAL TUBERCULOSIS ASSISTANCE

Question: The Committee remains concerned that certain identifiable locations, such as Honolulu and Florida, which have a disproportionate percentage of refugees or immigrants from Southeast Asia, continue to experience an extremely high incidence of active tuberculosis. Further, it is the Committee's understanding that efforts to increase surveillance or screening activities overseas do not address this problem since many of these cases are clinically "inactive" until the individual experiences psyco-social stress, such as that generated by leaving their homes and native culture. Accordingly, the Committee would appreciate learning to what extent the Department has given serious consideration to either requesting supplemental funds under its Preventive Health Service tuberculosis initiative authority, S 928 of the Budget Reconciliation Act of 1981, or if not, to target available discretionary funds to these "gateway" cities.

Answer: It is true that Hawaii and certain other States and cities experience substantial Asian immigration and refugee flow which impacts upon their overall tuberculosis problem. In Florida, there has been an impact from Haitian entrants. As part of the normal budget process, the Department has considered various options for providing tuberculosis assistance to the States. The Preventive Health and Health Services Block Grant was determined to be an appropriate, flexible mechanism, which is also consistent with the Administration's objective of consolidating categorical health programs into block grants which States can use to address their individual priorities. We anticipate that many States will continue to use block grant funds for their tuberculosis control programs.

PREVENTIVE MEDICINE RESIDENCIES

Question: Secretary Schweiker is very interested in Prevention, as am I. Wouldn't it be cost-effective to have more people trained in this field?

Answer: Yes it would be. A recent review article of the economic evidence on prevention ("A Review of the Economic Evidence on Prevention", Medical Care, May 1980, Vol. XVIII, No. 5. p. 473.), concluded that many preventive health measures indeed represent an efficient use of resources. Furthermore, it was concluded that the "actual value of prevention strategies may be understated since reductions in pain and suffering are usually omitted."

Question: What is the Department's priority for preventive medicine in general, and preventive medicine training specifically?

Answer: At a National Symposium ("Prevention and Medical Practice: The Role of Undergraduate Medical Education") on

October 6, 1981, Secretary Schweiker stated that prevention was a top priority of the Department. As a corollary to this, he stated that preventive medicine training would receive high priority within HHS. In implementing Section 793, grants for residency training, all types of fields of preventive medicine are eligible (i.e., general preventive medicine, public health, occupational health and aerospace medicine programs). However, the Department plans to propose a funding preference for general preventive medicine and public health residency programs that train individuals who are most needed to implement the Administration's health promotion and disease prevention initiative.

Question: How much money would be required for the Department to administer and carry out projects under this program?

Answer: The authorization level under P.L. 97-35 for residency training in preventive medicine (Section 793) is $1,000,000 for FY 1982, $1,500,000 for FY 83, and $2,000,000 for FY 84.

The goal of this program would be to assist in the continuing development and expansion of preventive medicine residency programs to train an additional 1,750 physicians in preventive medicine over a ten-year period to offset projected shortages.

Currently, there are only 363 physicians in training nationwide in preventive medicine residencies across all years of training (Source: American Colleges of Preventive Medicine, 1981). Preventive medicine typically requires 2-3 postgraduate years.

At present, the Continuing Resolution does not allow funds for new programs, although the 1982 President's Budget of $1,000,000 would enable the Department to support 10 residency programs training an estimated 30 residents.

Question: How many physicians with specialties in preventive medicine do you estimate the Nation will need in 1985 and 1990? How many do we have now?

Answer: The projected supply of physicians in 1990 in the specialty of preventive medicine has been estimated at 5,500 (GMENAC Report, Vol. II). While physician manpower needs in preventive medicine are difficult to measure, GMENAC future requirements estimates show a shortage of 1,750 preventive medicine physicians by 1990. Thus the 1985 shortage ranges between 1,500-1,650.

Question: How many physicians with specialties in preventive medicine does the Nation currently require?

Answer: It is common for practitioners to enter the field of preventive medicine at midcareer without returning for additional post graduate training or obtaining board certification. This fact makes it difficult to estimate the current supply and national requirement of physicians with specialties in preventive medicine, hence, there are no current estimates. The 1980 GMENAC Report stated that in order to meet 1990 requirement of 7,300 physicians with specialties in preventive medicine, an additional 1,750 would be needed.

Question: How many schools of medicine, osteopathy, and public health currently operate residency training programs in preventive medicine? How will they respond to this program if it is implemented?

Answer: A total of thirty-five schools of medicine (23 medical schools with one or more medicine residencies programs and 12 public health schools). Based on information in the annual report: "Medical Education in the United States, 1980-81" (JAMA, 246: 2939, Dec. 25, 1981), there are 77 accredited residency programs in preventive medicine in the U.S. In development of the implementation plan for Section 793 (Preventive Medicine Residency Training Program), there is reason to believe that the schools will respond positively to the implementation of the training programs.

SPECIAL HEALTH PROFESSIONS INITIATIVES

Question: It is my understanding that the Administration's initial proposal with respect to Special Health Professions Initiatives focused on keying the program into 5 or 6 specific areas. The Reconciliation Act authorized about 24 different areas under this program.

What is your view of the changes imposed by Reconciliation?

Answer: The Omnibus Reconciliation Act of 1981 added authorization for educational training projects in diabetes and other severe chronic diseases, dental education, and allied health personnel to the existing 21 areas authorized under the Special Initiative authority. The Administration's proposal in 1982 was to focus the program on five specific areas authorized under Section 788(b)-(e) for which the Administration is giving the highest priority. One of these areas related to education and training is the area of allied health personnel for health promotion and disease prevention, which is a new authority under this section. This initiative and the other four areas the Administration proposed to address did not receive funds under the 1982 Continuing Resolution. The Reconciliation Act repealed the separate authorities for dental education, the training of expanded function dental auxiliaries, and dental team practice, but added it under this broad discretionary authority along with the training of health professionals in the diagnosis, treatment and prevention of diabetes and other chronic diseases and their complications. In FY 1982, dental education will be funded under the General Dentistry Residency and Training Program to provide dental residents advanced skills in general practice of dentistry. The Nurse Practitioner, Advance Nurse Training, Public Health Preventive Medicine and Primary Care programs include an emphasis on diabetes and other severe chronic diseases as part of their educational curriculum and/or residency training.

Question: Do you support funding for the program as it is now constituted?

Answer: Yes, the program supports health professions projects in a number of high priority areas. These are:

1. education and training of allied health personnel for health promotion and disease prevention,

2. innovative projects to enhance the placement of podiatrists in underserved areas,
3. provision of clinical training to MODVOP students in areas that are geographically remote from the primary teaching facilities and where medically underserved populations reside,
4. development of systems for continuing education of practicing health professionals, especially those in medically underserved areas and those who provide primary care, and
5. improvement and strengthening of curricula in schools of veterinary medicine regarding care of food and fiber producing animals.

Question: Were all projects under the "old" curriculum program completed?

Answer: Due to approved budget rescissions in Fiscal Year 1981, a total of 76 continuation projects totaling approximately $7,200,000 were not funded during FY 1981. These projects included environmental/occupational health, geriatrics, nutrition, regional dental systems, and humanistic medicine & hospice care activities.

Question: To what extent should the program include projects for recruiting students in areas having shortages of Podiatric Manpower and for operating training programs in these shortage areas?

Answer: An additional 1,203 podiatrists were necessary in 1979 to bring the practitioner-to-population ratio up to 1:28,000. This ratio represents the number of podiatrists needed to treat foot conditions typically seen by podiatrists and was developed by the Health Resources Administration. In addition, approximately 73 percent of all counties in the U.S. do not have a podiatrist. To the extent that limited financial and other resources permit, podiatric medicine should be considered a high priority within this program.

GERIATRIC MEDICINE TRAINING

Question: How many more physicians trained in geriatric medicine does the Nation currently require?

Answer: The profession of medicine has not accepted geriatrics as a separate specialty, thus there are no residency programs in geriatrics. Although estimates of the number of trained geriatricians are not available, current body-of-knowledge does recognize a present shortage in geriatricians.

Question: How many more physicians trained in geriatric medicine will the Nation require in 1985, 1990, and 2000?

Answer: In the 1980 GMENAC Report, general internal medicine included diabetes, geriatrics and nutrition. GMENAC assumed the provision of services to the population over sixty-five will continue to be in the domain of general internists and family/general physicians since geriatrics is not a certified specialty. Therefore, we are unable to project requirements for this field of training.

Question: How many schools of medicine and osteopathy operate training programs in geriatric medicine?

Answer: Based on information in the August 1980 American Association of Medical Colleges Curriculum Directory, 81 of 132 reporting medical schools offered geriatrics courses in academic year 1980-81. Data on the number of schools that actually presented courses on geriatrics are not available. At least one program offers specialized clinical training in geriatrics at the graduate level.

Question: How many students complete their M.D. or D.O. and residency training with instruction in geriatric medicine?

Answer: From a 1977 survey of 363,619 active practitioners (88% response rate) only 629 physicians identified geriatrics as one of their areas of specialization. (Source: May 1980 Rand Report: Geriatrics in the U.S., Manpower Projections, and Training Considerations.)

SPECIAL HEALTH PROFESSIONS INITIATIVES

Question: I am troubled by the fact that while this hearing was expressly called to review new program authorities in the 1981 Omnibus Reconciliation Act, your testimony with respect to Special Health Professions Initiatives simply restates your March 10 budget justification in this area. It does not in any way address the specific new authorities for:

(a) curriculum development in geriatric medicine;

(b) developing the concept of teaching nursing homes in order to provide students with clinical training in geriatric medicine;

(c) training of health professionals in the diagnosis, treatment, and prevention of diabetes and other severe chronic diseases; and

(d) dental education.

Can you provide the Subcommittee with information regarding your plans to implement these new initiatives?

Answer: The Bureau of Health Professions is very interested in collaborating with the Administration on Aging, National Institute on Aging, Division of Long Term Care and other government agencies interested in geriatric medicine to provide adequate preparation of health professionals for the health care of the elderly. Under the old program of Health Professions Improvement and Development Projects, funds were awarded for curriculum development training for patient education programs for the elderly. The Nurse Practitioner, Advance Nurse Training, Nursing Special Projects and Primary Care programs include emphasis on programs for the elderly. These same programs plus Preventive Medicine and Public Health programs also include emphasis on diabetes and other severe chronic diseases as part of their educational curriculum and/or residency training. The 1982 Continuing Resolution has allowed $2,000,000 for dental education in the form of General Dentistry Residency and Training grants to provide dental residents advanced skills in general practice of dentistry.

Question: Under what statutory authority do you propose to conduct programs in curriculum development in schools of veterinary medicine?

Answer: Support for curriculum development in schools of veterinary medicine is authorized under Title VII, Section 788 (b) of the Public Health Service Act.

Question: In its report accompanying the FY 1982 Labor-HHS-Education Appropriations bill, this Committee expressed its concern about "the compelling need for health manpower development support in rural and underserved areas, as well as program development in geriatric and podiatric medicine." The Committee requested that the Department provide a report on its plan for meeting these needs at the Subcommittee's hearings on the FY 1983 budget. Is the Department prepared at this time to provide the Subcommittee with an update on this pressing concern?

Answer: In the 1982 President's Budget, the Bureau requested support for podiatric training under the Curriculum Development program authority. The President's FY 1982 budget also included funding of $1,000,000 for such projects. These programs were not included under the Continuing Resolution. Programs in rural and underserved areas as well as geriatric medicine are supported by a variety of health professions activities including the Area Health Education Centers (AHEC) program, Nursing, Physician Assistants program, and Family Medicine Residencies. Discussions concerning implementation of these type of programs in 1983 can be discussed at the 1983 Budget hearings.

Question: In your testimony you mention as a target area, innovative projects to increase the production of and enhance the placement of podiatrists in underserved areas. The reconciliation authority speaks very specifically to projects conducted by colleges of podiatric medicine to recruit students who reside in podiatric manpower shortage areas and to provide clinical training in such areas. Is it the Department's plan to include these two program elements in its "innovative projects?"

Answer: Yes, the implementation planning activities do include both elements.

Question: How does the Department plan to address the role of physicians in long-term care?

Answer: The movement toward training efforts in long-term care has been rather slow to develop, but it is picking up as the extent of the problem comes to be realized.

Even more than other segments of the population, the aged are affected by the fact that simple increases in the supply of health professionals do not necessarily result in there being enough trained personnel of the right types in the right places to provide needed services.

In the past, medical and nursing schools tended not to focus on care for the aged as a career. The prospects, it was believed, were too discouraging and unproductive. In recent years, however, examination of the aging process (gerontology) and of diseases of old age (geriatrics) has led to a renewed interest and hope.

In the field of medicine, there has been some movement toward incorporating geriatrics into medical school curricula, according to the Rand study on geriatrics.[1] As late as a few years ago, in 1976, the Senate Special Committee on Aging in a survey found that only 3 of 87 responding schools had established geriatrics as a specialty within the curriculum.

In another 1976 survey by Akpom and Mayer, 15 of the 96 respondent schools indicated that they taught geriatrics as a separate subject, and only two made it a mandatory part of the curriculum.

Based on more recent data, the Rand study concludes that:

> "...by June 1979, a total of 61 U.S. medical schools offered courses in geriatrics, gerontology, or both to medical students. Of these, 4 now mandate a clerkship in geriatric medicine or psychiatry and an additional 4 include geriatrics as part of a major clinical clerkship. In addition to these 8, another 21 intersperse didactic material in geriatrics or gerontology through the preclinical and clinical years as part of other courses. In 55 of the 61 schools, elective courses are offered; most of them are clinical clerkships of one kind or another."

Geriatrics is also being addressed increasingly in terms of residency and fellowship programs. The Rand study cites some 25 residency programs in family practice that provide opportunities in geriatrics. Another 18 internal medicine residencies have developed or will develop block-time rotations in geriatric medicine.

Not only have attitudes been changing as more encouraging prognoses become apparent, but programs are being developed in Federal and State agencies.

Among the program efforts carried out by the Bureau of Health Professions in HRA aimed at training or health professions development to meet long-term care needs are the following:

- Training grants for primary care residencies (family practice and internal medicine) include elements of programs for the elderly. Each Federally funded program must have a planned curriculum that emphasizes subjects pertaining to ambulatory care, such as management of geriatric patients and recognition and treatment of chronic illness; and subjects pertaining to pyschosocial skills, such as management of terminal illness.

- The Bureau has funded a series of grants to support the development, implementation, and evaluation of new geriatric course materials and curriculum improvements. These were at a level of about $2.1 million in FY 1979 and $1.6 million in FY 1980, with approximately half the grants going to schools of medicine and the remainder given to schools of dentistry, optometry, pharmacy, public health, etc. During 1981 and 1982, no funds were appropriated for curriculum development.

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[1] Rand Corporation, Geriatrics in the United States: Manpower Projections and Training Considerations (R-2543-HJK), May 1980.

The PHS Long-Term Care Workgroup under the leadership of the Surgeon General, has just been initiated, with the first meeting held in December 1981. Over the next year, this group will review a number of alternative approaches to dealing with long-term care problems. They will also review potential priorities for the next budget cycle.

PACIFIC BASIN AREA AID

Question: During its deliberations on the Department's Fiscal Year 1982 Appropriations Bill, the Committee heard public testimony from the Dean of the University of Hawaii's Schools of Medicine describing the truly unique health and rehabilitation needs of the Pacific Basin; for example, that in Ponape and Kosrae, the incidence of childhood leukemia is ten times the expected rate. The Committee subsequently "strongly encouraged" the Health Resources Administration to give every consideration to addressing these pressing needs, especially given our international treaty obligations to provide such care.

Accordingly, the Committee would appreciate learning what specific activities the Health Resources Administration has undertaken, or plans to undertake, this fiscal year in response to the Committee's interest.

Answer: In the past, we have provided health professions education funding to the Pacific Basin Area through such programs as health professions educational projects, family medicine training programs, nursing special projects, public health, and disadvantaged assistance. In FY 1982, over $500,000 will be provided to the Pacific Basin Area to help support their health professions training needs.

PUBLIC HEALTH EMERGENCY RESPONSE FUND

Question: Under the Public Health Service Act, the Public Health Service has an on-going responsibility to provide prompt and effective assistance to States and other Federal agencies in emergency situations which pose an immediate threat to the public health.

Does the Department plan to request funding for the Public Health Emergency Response Fund for fiscal year 1983?

Answer: Our FY 1983 budget request does not include resources for the Emergency Response Fund. Although in a number of cases in the past few years we have been called upon to respond to unanticipated emergencies, we have done so successfully and effectively. Our success, in part, has been due to the availability of resources from a variety of sources. The Centers for Disease Control provides technical assistance to states during epidemic situations. The Federal Emergency Management Agency made funds available for Cuban refugees. Congress provided resources for Mt. St. Helen's, Love Canal and refugees. Furthermore, Superfund resources from the Environmental Protection Agency are now available in the event of toxic substance emergencies.

Question: By what method do you calculate the amount of money required for this purpose?

Answer: We are not requesting resources in FY 1983 for the Emergency Response Fund.

Question: Will guidelines be established for the expenditures of these funds?

Answer: Although we are not requesting resources for this program, sufficient guidelines exist in the Public Health Service Act and our administrative and financial management procedures.

Question: Are there any other sources of funds in the Department that could be used for emergency response activities?

Answer: As in the past few year, HHS is capable of responding to state requests for assistance in public health emergencies. The Centers for Disease Control maintains an ongoing effort to help localities in identifying and controlling disease outbreaks such as Legionnaire's Disease and Toxic Shock Syndrome. The Food and Drug Administration has also assisted in public health emergencies such as Toxic Shock Syndrome and Three Mile Island. The National Institutes of Health has played an active role in situations requiring highly technical biomedical assistance such as testing of chemicals in Love Canal.

Question: Are there other Federal agencies, such as the Federal Emergency Management Agency, which currently provide health related disaster assistance?

Answer: Resources from the Federal Emergency Management Agency and the Environmental Protection Agency are currently available to HHS to provide health related disaster assistance to states and localities in areas where HHS does not have ongoing programs.

We are in the process of negotiating with EPA on the scope of HHS activities that can be carried out within the appropriated resources for Superfund. These funds will enable HHS to protect the public health and ensure worker safety through the following activities:

> Scientific Support (Lead PHS Agency: CDC) provides technical consultation, field manuals, training of state and local health officials and review of all environmental test results conducted at EPA site investigations.
>
> Emergency Response (Lead PHS agency: CDC) provides expertise and laboratory support at emergency sites and negotiates agreements with States to provide additional staff if needed during emergency situations.
>
> Health Studies (Lead PHS agency: CDC) supports health assessments and health studies on the implications of exposure to toxic substances (1982 sites include: Hollywood/Memphis, TN; Triana, AL; Old Forge, PA; Woburn, MA; and Love Canal)

Health Surveys/Investigations (Lead PHS agency: CDC) includes development of guidelines/protocals for needed laboratory and/or epidemiologic investigations for basic studies such as chromosome or mutagenic surveys, reproductive outcomes, and standard tests for liver functions. Supports health surveys, studies and/or registries of EPA-designated dump sites.

Worker Safety and Health (Lead PHS agency: NIOSH) includes development of worker safety guidelines and manuals; design of worker safety plans for specific sites as requested by EPA.

Toxicology Data Bases (Lead PHS Agency: National Library of Medicine and National Toxicology Program) supports computer data base on human health effects of exposure to toxic chemicals, and short-term toxicological testing of priority chemicals or chemical combinations for which no health effects data exists.

Question: What provision will be made for disposition of any of these emergency funds that are not expended at the end of the fiscal year?

Answer: We are not requesting resources in FY 1983 for the Emergency Response Fund.

Question: If health-related emergencies requiring Department activities during the fiscal year necessitate the expenditure of more money than is appropriated for this purpose, how will they be funded?

Answer: An emergency supplemental request would be submitted to Congress if the extent of the public health emergency requires additional resources for an effective Departmental response beyond the current resources appropriated.

SUBCOMMITTEE RECESS

Senator SCHMITT. The subcommittee will stand in recess, subject to the call of the Chair.

[Whereupon, at 3:30 p.m., Wednesday, February 3, the subcommittee was recessed, to reconvene at 8:30 a.m., Thursday, February 11.]

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 1983

MONDAY, MARCH 2, 1982

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, D.C.

The subcommittee met at 9:35 a.m. in room 1114, Everett McKinley Dirksen Senate Office Building, Hon. Mark O. Hatfield presiding.

Present: Senator Hatfield.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

CENTERS FOR DISEASE CONTROL

STATEMENT OF DR. WILLIAM H. FOEGE, DIRECTOR

ACCOMPANIED BY:

- **DR. GEORGE E. HARDY, JR., ASSISTANT DIRECTOR/WASHINGTON**
- **JAMES D. BLOOM, EXECUTIVE OFFICER**
- **DR. JOHN D. MILLAR, DIRECTOR, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFTY AND HEALTH**
- **CLAUDE F. PICKELSIMER, JR., DIRECTOR, FINANCIAL MANAGEMENT OFFICE**
- **ANTHONY L. ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

SUBCOMMITTEE PROCEDURE

Chairman HATFIELD. The subcommittee will come to order. This morning we will continue our fiscal 1983 hearings for the HHS Appropriations Subcommittee. Today we will hear testimony from the Centers for Disease Control, which is a key agency within the Department of Health and Human Services, having an important mission of protecting the Nation's health, tracking down diseases, and protecting American workers from occupation-related illness and injury, and a host of other purposes.

I personally believe that preventing the incidence of unnecessary illness, mortality, and assisting States to do the same is perhaps the most important function of the Federal Government in the health area. It is not an area where we can afford to cut corners, even in a tight budget year.

We do have the ongoing responsibility to see that funds are well spent in accordance with Federal national health priorities. In fact, I believe I read an article not too long ago that indicated of all the Federal dollars expended, the ones that have the greatest multiplying impact in the general economy are the dollars spent in this area, of all the Federal tax dollars spent.

We are pleased to have with us today Dr. William Foege, Director of CDC. Dr. Foege, please introduce the people you have with you, and your entire statement will be placed in the record and you may proceed as you wish. You may summarize.

INTRODUCTION OF ASSOCIATES

Dr. FOEGE. Thank you, Mr. Chairman. On my far right is Mr. Tony Itteilag, the Deputy Assistant Secretary for Budget with the Department; Dr. Millar, Director of NIOSH; and Mr. Jim Bloom, the Executive Officer of CDC.

I will simply summarize some of the highlights of our opening statement.

PREPARED STATEMENT

Chairman HATFIELD. Your statement will be put in the record.

[The statement follows:]

Statement of William H. Foege, M.D.

Mr. Chairman and members of the Committee: At the Centers for Disease Control during the past year, our program activities have been developed and carried out within the framework of: (1) The 1990 Preventive Health objectives for the Nation; (2) The priorities outlined in the 1979 Surgeon General's report, Healthy People; and (3) The recent realignment of Federal/State responsibilities which places greater responsibility with the States, and increases the importance of CDC's role as a scientific and technical resource for the Nation.

HIGHLIGHTS

I would like to review some of the highlights of this past year:

CHARTS 1 and 2

- The Childhood Immunization Initiative continues to be one of our most outstanding programs. Working in concert with State and local workers, we can report that immunity levels have never been higher and the incidence levels of vaccine-preventable diseases have never been lower. This has been achieved through the combined efforts of public, private, and voluntary workers at all levels--national, State, and local. Capitalizing on the decreased backlog of unimmunized children, the greatly expanded involvement of voluntary groups, and the well established and highly efficient immunization systems that have been developed in State and local health departments, the objective of interrupting indigenous transmission of measles by October 1982 appears attainable.

CHART 3

- Last year, I reported on a new disease called "Toxic Shock Syndrome (TSS)." The monthly reported incidence of TSS continued a decline which began in September 1980, and the case-fatality ratio declined from 5.1 percent in 1980 to 3.3 percent in 1981.

CHART 4

  Today I have to report on our involvement in another unusual and serious health problem--Kaposi's sarcoma and opportunistic infections in young men. Kaposi's sarcoma is a rare malignancy that is usually seen in elderly men. At the same time, we were seeing evidence of other problems among males--Pneumocystis pneumonia and other fatal infections previously seen only among persons with immunodeficiences, and other unusual cancers and problems in young men. In this country, Pneumocystis pneumonia (PCP) was thought to be almost exclusively limited to severely immunosuppressed patients. Since mid-June there have been 235 reported cases and 94 deaths from these illnesses. To date, the reservoir of illness has been among young males. We must learn about the problem, especially the potential for spread of these illnesses. We have formed a special task force at CDC, made up of various specialists, which has developed a surveillance system, conducted field interviews, and is undertaking case-control studies in these problems.

- In May, Spanish health authorities asked CDC to assist with a health problem involving atypical pneumonia in communities near Madrid. By mid-October, the death toll had reached more than 160, with deaths occurring at a rate of nearly one per day. The outbreak had originally been thought to be caused by an infectious organism or toxic agent. Our investigation is considering all possibilities.

- In addition to assisting with the toxic pneumonia problem in Spain, CDC's environmental health scientists have been investigating PCP contamination in Binghamton, New York, Old Forge, Pennsylvania, and New Bedford, Massachusetts, and assisting in identifying health risks of a pesticide spraying program in California. Less dramatic, but of critical importance, is the work that has been done to develop new and improved laboratory techniques to measure thirty known toxic substances in humans.

- CDC's Center for Environmental Health and NIOSH have specific responsibilities related to the Comprehensive Environmental Response, Compensation, and Liability Act, referred to as the Superfund. In addition, CDC was given lead responsibility in HHS for coordinating the Department's involvement in the Superfund. We have established a Superfund office in our Center for Environmental Health, from which we are coordinating the efforts of the National Library of Medicine, and the National Toxicology Program. These activities will be carried out on a reimbursable basis with funds appropriated to the Environmental Protection Agency (EPA). We are in the process of negotiating the scope of HHS activities that can be carried out within those appropriated funds.

- Also, I would like to bring you up to date in a few scientific areas that I reported on last year. We recently marked the fifth anniversary of the isolation of the Legionnaires' Disease organism. Since then our investigations have implicated a number of environmental sources of outbreaks and our efforts have led to the identification of eight new named species of Legionella, and nine other species which need more thorough definition.

  Last year, I reported that we were conducting field trials of a promising hepatitis B vaccine. The vaccine has shown to be highly efficacious and safe and has been licensed by the Food and Drug Administration. We are continuing our work on a vaccine for hepatitis A. A live vaccine is expected to be ready for field testing this fiscal year.

  We have continued to apply the revolutionary hybridoma technique to produce new, pure monoclonal antibodies for our diagnostic procedures. To date, nearly 20 sets of monoclonal antibodies have been developed for particular microorganisms.

- During the year, we completed the initial development of, and tested, a threat assessment system, which has been established in cooperation with the Department of State and the Department of Justice. With this system in place, enforcement agencies can call on CDC to assist them in obtaining a rapid assessment of the scientific, technical, and behavioral probabilities of a situation involving the threatened hostile use of biological and chemical agents. Within minutes, the system can marshall the scientific competence of CDC, Fort Deitrick, the Chemical Systems Laboratory at Edgewood Arsenal, and a special outstanding behaviorial team that is on stand-by. The threat assessment system, when added to existing resources--our surveillance systems, our highly specialized laboratories and unique scientific competence, and our Epidemic Intelligence Service--gives us a more responsive and comprehensive civilian defense against the accidental or intentional exposure of our population to chemicals or biological agents.

1983 BUDGET REQUEST

The 1983 budget reflects the changing Federal/State roles, but the request also reflects the importance of the programs and the activities in Preventive Health Services in reaching 1990 objectives. Our budget request is for $217,192,000.

Venereal Diseases

We are requesting an increase of nearly $8.6 million in our Venereal Disease Grant Program, restoring it to the 1981 funding level. By adjusting budget periods of grant awards during 1982, we will be able to avoid disruption in State venereal disease programs during the current fiscal year. It is important that we not lose momentum. That the program is working is seen in decreasing gonorrhea rates. A decrease of about $1.8 is million proposed for the direct operations portion of our venereal disease activities. We will focus our in-house efforts on areas of highest priority, such as surveillance, research and investigation of syphilis, penicillin resistant gonorrhea, and pelvic inflammatory disease. The reduction will primarily be in our work on the herpes virus.

CHART 5

Risk Reduction/Health Education

$1.3 million is requested to continue our work on the development, evaluation, and application of effective health education and risk reduction interventions. During 1982, we will be supporting these activities with funds available under the block grant support as directed by Congress. At the end of this transition year the block grant is being transferred from our appropriation to funding in the Office of the Assistant Secretary for Health. This request will support staff to provide States and other public and private health education sponsors with expert technical assistance to implement effective health education programs.

Occupational Safety and Health

This budget continues the course set in 1982 toward targeting further limiting occupational safety and health research to the highest priority areas--surveillance, the evaluation of occupational safety and health problems (including response to requests for Health Hazard Evaluations), and the control of occupational safety problems. Also, the occupational safety and health training program is proposed for termination. Let me assure you that the prevention of illness and death in the workplace is high on my priorities. I believe we must concentrate on strengthening NIOSH scientific investigations and improving our information gathering. For example, NIOSH, in conjunction with the Consumer Product Safety Commission, recently developed a new surveillance system to monitor all occupational injuries treated at a sample of 66 hospital emergency rooms. With this new system, we should be better able to estimate injury patterns of the American worker on a more current basis than is now possible.

Preserving Scientific and Technical Operations

Of major significance in this budget is the funding that has being provided in 1982 and requested in 1983, which has preserved the scientific and technical core supported in the Chronic Disease, Environmental Health, Epidemic Services, and Technical Development and Application activities of our budget. In 1982, $10.7 million is being allocated from the PHS termination account to supplement these activities and avoid a serious disruption in these disease control efforts. We believe this is consistent with Congressional intent under the continuing resolution. Without this transfer, CDC would have had to conduct a reduction in force of approximately 420 employees, that would have affected all of its components except NIOSH. Such an employment reduction would have cut deeply into the professional, technical, and support personnel who are responsible for making CDC the responsive public health agency that it is. While it will still be necessary to implement a number of economy measures, we will be preserving the Centers' core operations. Also, consideration will be given to the October 1981 pay raise requirement in March 1982.

I am happy to answer any questions that you may have.

CHART NO. 1—IMMUNIZATION BACKLOG—SCHOOL AGE CHILDREN

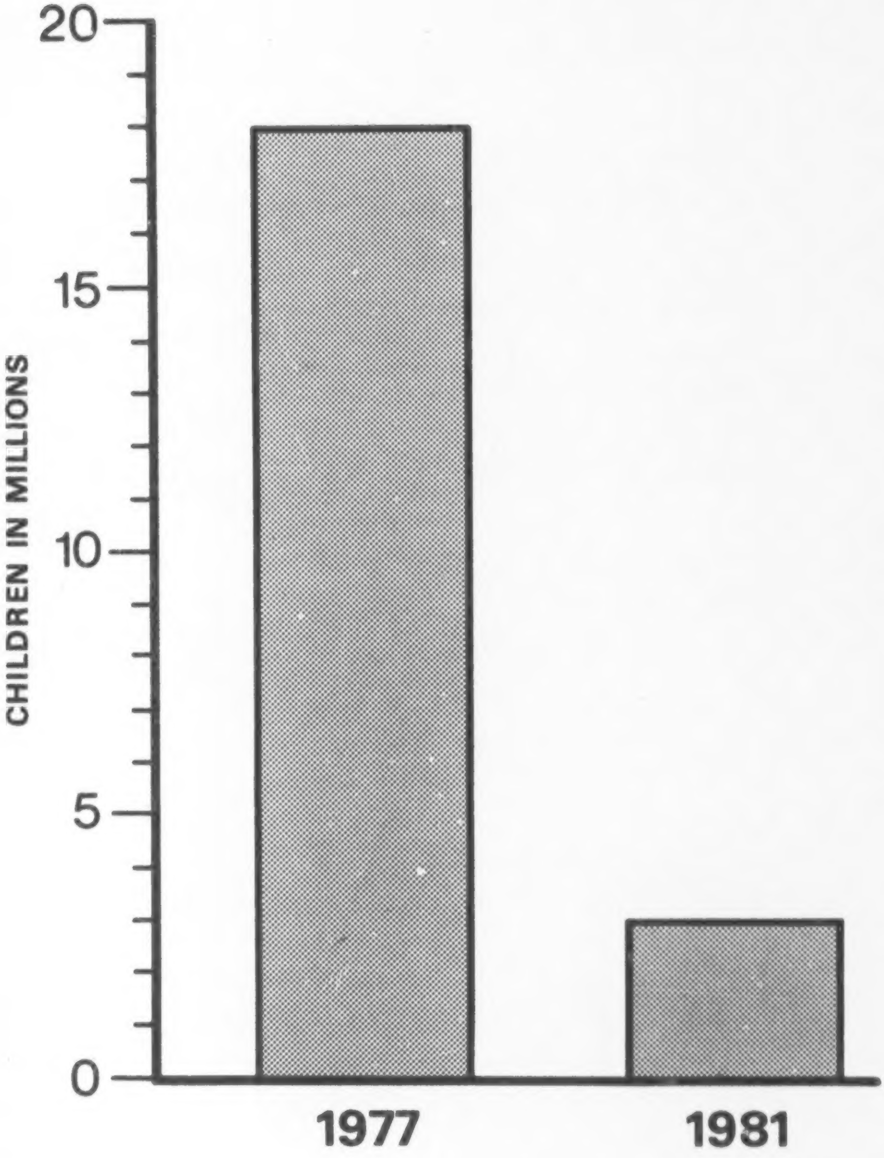


CHART NO. 2—REPORTED MEASLES MORBIDITY

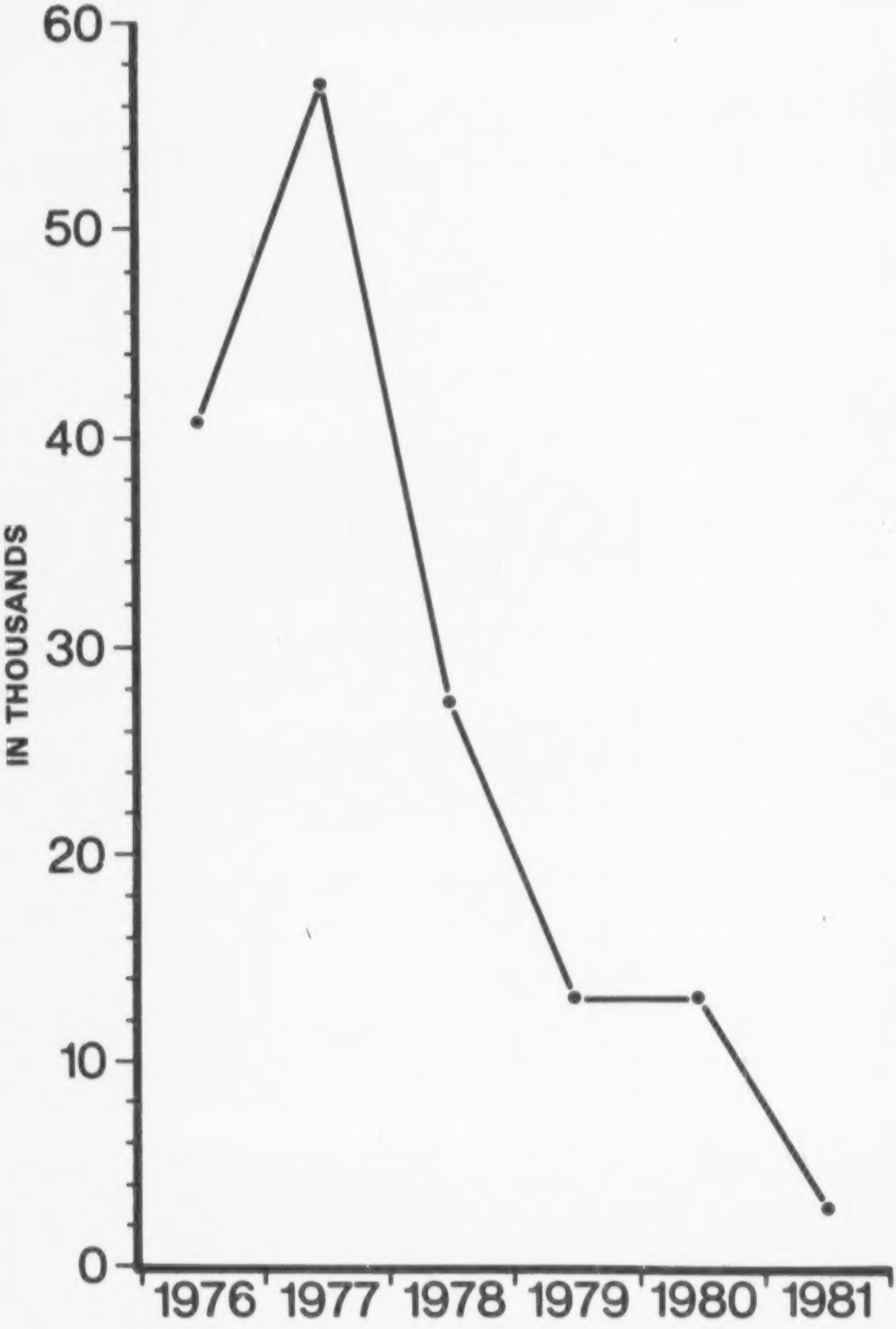


Chart No. 3—Toxic-Shock

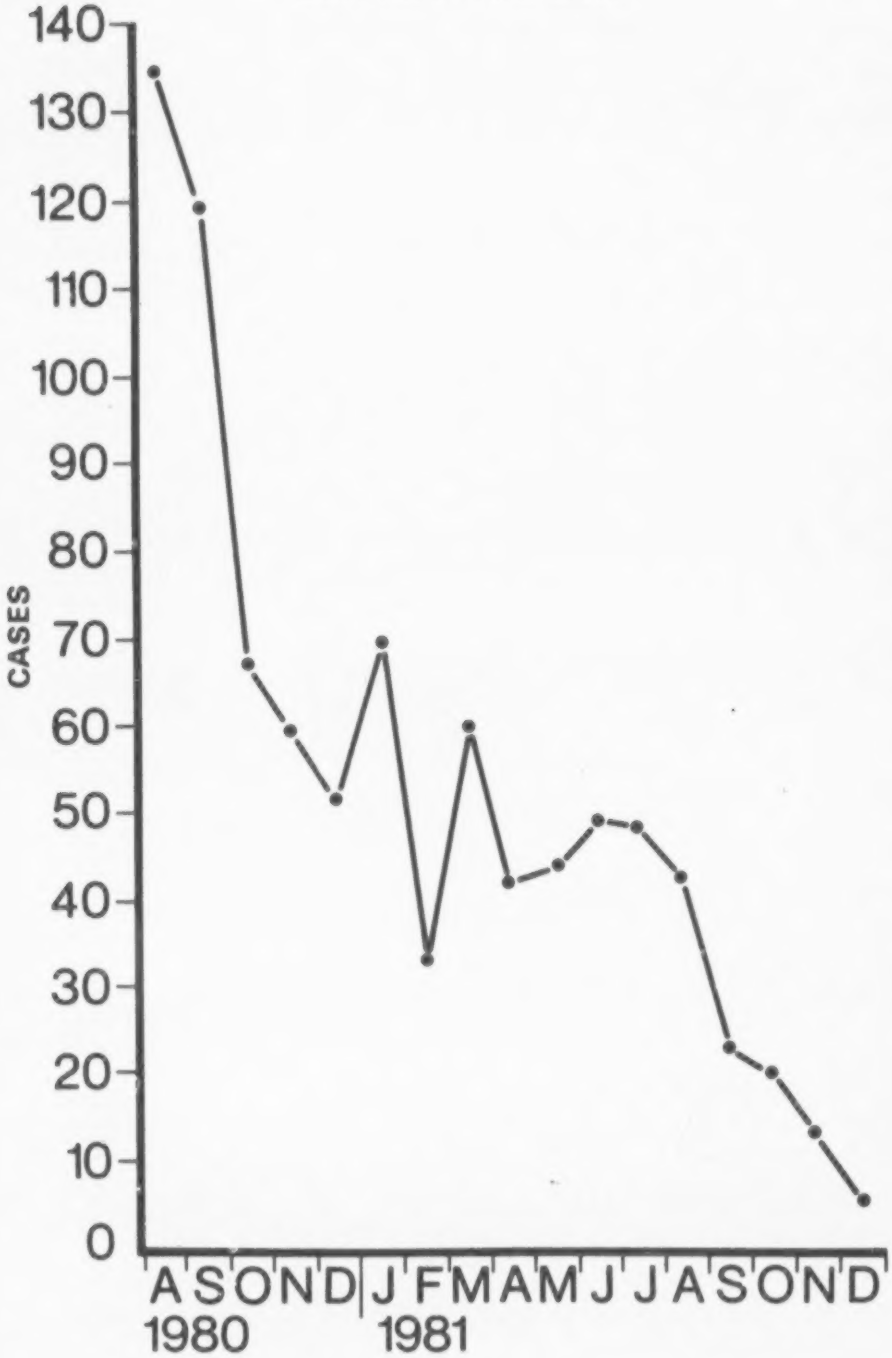


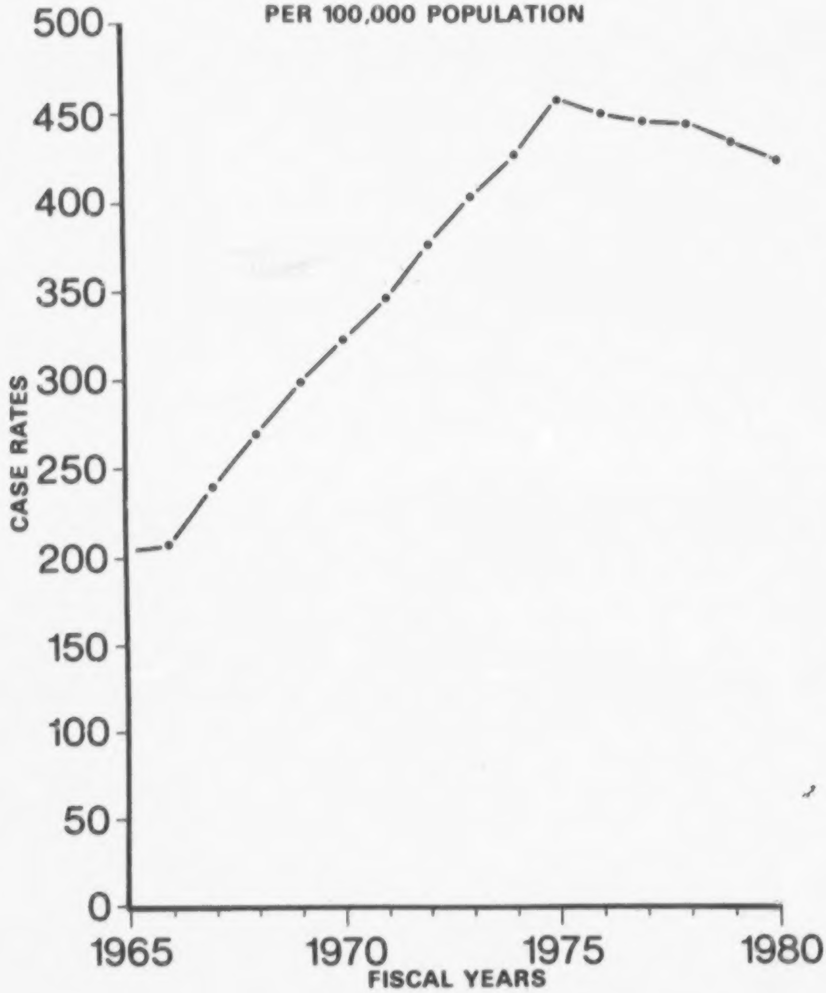
CHART NO. 4—KAPOSI'S SARCOMA AND OPPORTUNISTIC INFECTIONS

JUNE 1, 1981 - FEBRUARY 3, 1982

	Total Cases	Deaths
Kaposi's Sarcoma	95	15
Pneumocystis Pneumonia	102	57
Kaposi's and Pneumocystis	20	13
Other	18	9
TOTAL	235	94

CHART NO. 5—AGE-ADJUSTED GONORRHEA

PER 100,000 POPULATION



BIOGRAPHICAL SKETCH

NAME : William H. Foege, M.D.

POSITION : Director, Centers for Disease Control

BIRTHPLACE AND DATE : Decorah, Iowa, March 12, 1936

EDUCATION : Pacific Lutheran University, 1957, B.A.

University of Washington Medical School, 1961, M.D.

Harvard University, 1965, M.P.H.

EXPERIENCE

1977-Present : Director, Centers for Disease Control, Atlanta, Georgia

1976-1977 : Assistant Director for Operations, Center for Disease Control

1975-1976 : Assistant to the Director, Center for Disease Control

1973-1975 : Medical Officer, World Health Organization, New Delhi, India

1970-1973 : Director, Smallpox Eradication Program, Center for Disease Control

1969-1970 : Chief, International Branch, Smallpox Eradication Program, National Communicable Disease Center

1968-1969 : Chief of Operations Area B, Nigeria, Dahomey, Togo, and Ghana, Smallpox Eradication/Measles Control Program, National Communicable Disease Center

1966-1967 : Epidemiologist, Smallpox Eradication/Measles Control Program, Eastern Nigeria

1965-1966 : Medical Officer, Immanuel Medical Center, Yahe, Eastern Nigeria

1962-1964 : Epidemic Intelligence Service, Communicable Disease Center

1961-1962 : Intern, USPHS Hospital, Staten Island, New York

1967-1976 : World Health Organization Consultant

TEACHING APPOINTMENTS : Visiting Lecturer on Tropical Public Health in the School of Public Health, Harvard Medical School, Boston, Massachusetts

Clinical Professor, School of Medicine, Emory University, Atlanta, Georgia

ASSOCIATION MEMBERSHIPS : American Epidemiology Society

American Public Health Association

American College of Preventive Medicine

American Medical Association

American Association for the Advancement of Science

Royal Society of Tropical Medicine and Hygiene

Indian Society for Malaria and Other Communicable Diseases

HONORS : Honorary Doctor of Science, Tulane University, 1980.

Recipient of the University of Washington School of Medicine Distinguished Alumnus Award, 1979.

Honorary Doctor of Laws, Valparaiso University, 1978.

Recipient of the 1978 Joseph C. Wilson Award for achievement and promise in international affairs.

Honorary Doctor of Science, California Lutheran College, 1977.

Recipient of the Pacific Lutheran University's Distinguished Alumnus Award, 1976.

CDC Special Achievement Award, March 1975.

PHS Superior Service Award, May 1970.

Delta Omega, 1965.

Honorary Doctor of Science, Wartburg College, 1979.

OVERVIEW

Dr. FOEGE. Our testimony on 1982 and 1983 is based upon the 1990 objectives for the Nation that were drawn up in the last 3 years by groups from around the country and the Surgeon General's report on prevention.

Several of the highlights in the last year are worth mentioning, the first one being the immunization program for the vaccine preventable diseases of childhood. I am very pleased that we have improved an already good program. You can see by the first chart that the backlog of children inadequately immunized has decreased from about 18 million school age children in 1977 to about 3 million in 1981. At the same time we see a marked reduction in the actual incidence of those diseases.

Next chart, please.

In 1980, we had a record low number of measles cases in this country, with 13,500. In 1981 we have gone far below that to just slightly over 3,000 cases, and so far in 1982 we are even below the 1981 level. We are coming very close to being able to interrupt the transmission of measles in this country. We will continue to have the importations, and, indeed, we have two to three importations a week into this country from other countries. But we believe it will be possible within this next year to eliminate indigenous transmission and then handle each importation as it occurs.

I might say on measles—you were mentioning the benefits that are derived from prevention programs—since the measles program started in the 1960's, not only have we saved thousands of lives, but there are about 15,000 children in this country who are not retarded who would have been retarded without the measles program. The benefits to this country are such that in 1982 the returns from just this part of the vaccine program, just measles, will exceed the entire budget of CDC.

We now have 50 States with school entry laws, so that a child cannot enter school without being properly immunized, unless there is a medical or religious reason for not being immunized. And 39 States require any child from kindergarten to 12th grade, so that even if they move from one school to another they have to show proof of immunization.

Last year we reported on a new condition, toxic shock syndrome. While there are still many unanswered questions, we see a gratifying drop in the number of cases of toxic shock syndrome. We have had a total of about 1,400 cases with 80 deaths reported since this was first recognized in 1980.

Today we report on another new condition that is an unexpected public health problem. We are finding a rare tumor, Kaposi's sarcoma, which normally was not seen frequently, and when seen, was usually in older men. Kaposi's sarcoma is now being seen in young men. Oftentimes a very rare infectious disease, pneumocystis pneumonia, and other "opportunistic" infections usually found in people who have underlying immunological defects are also being found in young men. Since June 1981 we have had 234 cases reported with 94 deaths, primarily in young males.

In the area of occupational and environmental health, we have continued to deal with a wide spectrum of problems, including injury control in and out of the workplace. We are now using a special surveillance technique based on the emergency room experiences. We have continued to look at health effects of agent orange, both for those people involved in producing agent orange and those also using it. We have continued to monitor lead levels for occupational exposure and nonoccupational exposure. And part of the favorable news in this area is that the nationwide survey has shown a reduction in the average lead level in the population in general in this country, which we believe is due to the decreased use of leaded gasoline.

Our 1983 budget has only two program increments. One of the program increments has to do with venereal disease, where we are requesting an increase of $8.6 million in VD grants and a simultaneous decrease of $1.8 million for the direct venereal disease operations.

We can only report that we have a sustained decrease in the rate of gonorrhea in this country. The venereal disease problem as a whole is still a very large one, with about 10 million cases a year. With gonorrhea, we are having, however, a reduction in the last few years, and this is despite surveys which show an increase in sexual activity of teenagers. We are happy to see this reduction. To maintain the trend, we are asking for an increase in funding in venereal disease.

The second and only other program increase that we are requesting is for $1.3 million to continue our work on risk reduction. We believe that what people do to and for themselves can be as important now as all of 20th century science. We believe it is important to find better techniques to get that message across to the population.

For example, at my age I can expect only six additional years of life, as compared to my grandfather at the same age. But it has been found in studies in California that a person my age using simple health habits—not smoking, drinking in moderation, good diet, exercise, and so forth—can have 10 to 11 years more life expectancy than a person my age not doing that. That means what we do for ourselves can be more powerful than 20th century science, and we are asking for $1.3 million to conduct a program to get that message effectively across.

With this short statement, Mr. Chairman, I will stop and would be pleased to answer your questions.

BUDGET REQUEST

Chairman HATFIELD. Thank you very much, Dr. Foege. You have an awesome responsibility to oversee the Federal preventive disease control or retardation. I cannot but notice that your total budget request for CDC activities, if you include the block-grant funding, is just under $300 million, which is less than the cost of one fully outfitted B–1 bomber. Your program funding has remained relatively level, while virtually every area in the defense budget is slated for sizable increases.

At the fiscal year 1983 budget request level, how strong will our disease prevention arsenal be?

Dr. FOEGE. We will attempt, Mr. Chairman, to maintain the core scientific capability that is available to help States with technical assistance. As you know, many of the activities that we have been involved in before directly will now be given to States through the block grant, but we will remain available to help them.

We think the core scientific capability will remain strong.

Chairman HATFIELD. Would you like to make any general assessment on the capability at the State level to assume these roles, these new designed roles through the block-grant program?

Dr. FOEGE. I have no question that the State and local health departments have not only improved their capabilities, but they are the place for running most of these programs.

They, as the Federal Government, are faced with severe fiscal restraints, and I think it is important to see that historically about two-thirds of all of the prevention money in this country has come from State and local sources rather than from Federal sources. So that is still the major source of funding. And I would hope that they would be able to maintain the sort of programs that they have been doing.

Chairman HATFIELD. What was the budget level you initially requested, as it was presented to OMB?

Mr. ITTEILAG. Let's put that in the record. I have it here, but I do not know. It would take a couple of minutes to dig it out.

Chairman HATFIELD. OK. Would you find it, please?

[The information follows:]

BUDGET REQUEST TO OMB

The budget request to OMB for fiscal year 1983 preventive health services was $339,885,000. This request included $97,500,000 for preventive health and health services block grants, which program is now included in the congressional budget request for the Office of Assistant Secretary for Health.

BLOCK GRANTS

Chairman HATFIELD. Dr. Foege, in looking at the centralization, the transfer to OASH, it would appear that the expertise of the CDC staff would be lost in the process. What steps do you propose to take to make certain that the staff handling the administration block of OASH would be knowledgeable about preventive programs?

Dr. FOEGE. I have discussed this with Dr. Brandt, Assistant Secretary for Health. Since a number of the block grants will be centralized, we expect some efficiencies in being able to handle programs because of the centralization.

The technical assistance is an area that concerns him as well as me. We have agreed that he will use the CDC staff for the technical assistance, for analyzing the programs that the States propose. We believe that we will be able to continue much as we have in the past.

Chairman HATFIELD. If I am not mistaken, some States are delaying the action as far as participation in this block grant. Can you either confirm or refute this impression that I have; and, if it is true, why are they delaying participation?

Dr. FOEGE. I believe there are four programs that have delayed entry. Most of them have plans to enter before October of this year, and some of them have done this simply because it is easier with their own process to continue getting categorical money until this fall. I believe by this fall all programs will be participating.

Chairman HATFIELD. So this is a transitional problem?

Mr. BLOOM. There were 51 States that had applied for the block grant during the first quarter of this year, the prevention block grant.

Chairman HATFIELD. Are you aware of any States not using prevention service funds for the purposes established in the law?

Dr. FOEGE. I am not, but that is probably because we do not yet have good information on how the States are actually using the 1982 money. I would not want my answer to be a reflection of what has actually happened. We just do not have the information.

Chairman HATFIELD. Are you in any process of gathering that information?

Dr. FOEGE. Given the way the block grant is constructed, the policy of the Department is not to require any information that is not actually asked for. Therefore, we will not have a system that demands reporting on the part of the States. The reporting that we will get will turn out to be voluntary reporting from the States.

Chairman HATFIELD. What would happen to the States if they were not using such funds for prevention service programs? Would that not be in violation of the law?

Mr. BLOOM. I believe the legislation is set up so that if the States are not using the funds in accordance with the law, then future awards would be withheld from that State.

Chairman HATFIELD. In other words, if the States failed to obey this, they would be prevented from using funds for other programs? If they are not using it for that program, withholding will not be any penalty.

Mr. BLOOM. It would just be a matter of not granting the funds, their allocation under the block grant, so that they could not misdirect those funds, if, in fact, that were the case.

Chairman HATFIELD. How do you know that they are failing to do this? You have no mechanism or information organization, as I understand it, to ascertain failure on the part of the States in this particular area.

Mr. BLOOM. The legislation requires an annual audit to be conducted by the State itself. The Department, it is my understanding, plans to do selective program reviews of the block grants out of their Office of Inspector General, I believe. In addition, there is the annual application and an annual general program review before they will come in. There is also a requirement that the States are to hold legislative hearings on the grants.

So there will be a public record available for review. Within the block grant, though, the only specification after the first year is going to be the categorical program for services for rape victims.

ACCOUNTABILITY

Chairman HATFIELD. What I hear may not be accurate, but it seems to me we do not actually have a rule of accountability in this particular program, or a method of accountability. This is fairly haphazard in terms of following through on States.

Mr. BLOOM. It is my understanding of the philosophy behind the block grant that the intention was to provide as much flexibility as possible in the use of these funds. The nature of the accountability that has been built into the legislation is in line with that kind of flexibility. It does not require preplanning and accounting against a plan. It says to the States to establish your own priorities and, with the exception of services to rape victims, use the funds in accordance with your own priorities.

But you are right, there is not strict accountability, as we have with many of the other programs.

Chairman HATFIELD. I would like to go on record here indicating my understanding of Webster on "flexibility" and "accountability." I see no dichotomy. Rather I think that there can be flexibility in administering a program to encourage the greatest degree of creativity and so forth, and still have very strict accountability.

I do not think the block grant, moving from categorical to block grant, was in any way intended to create a lesser degree of accountability, even though it may be extended more with greater incident at the State and local levels than at the Federal level. I just do not think that there is any—should be any lessening of accountability under the various formats.

If you feel that there is call for defining the legislative intent or authority that you may feel lacking on your part to demand accountability or to develop a system of accountability, more precise than what you appear to feel that you have now, I would be happy to consider an amendment or whatever is necessary legislatively to develop that.

Why don't you look at this over the next few months and see if there is any lack of authority or any lack of understanding of legislative intent? We might create more accountability this way. Or maybe you don't feel the need of it. It just seems to me in this brief little colloquy that I think that this is sort of a vague, ill-defined area that could drop easily between the cracks between the States' and the Federal Government's individual roles.

Dr. FOEGE. Well, the States have to come in with a plan on how they will spend money. There is no provision for then verifying that that is the way it was spent, but the State health officers themselves are becoming concerned about this, and they are trying to develop a voluntary system that they would all agree to follow for a public health program reporting system.

Chairman HATFIELD. That would be fine. I'm not clear on the idea that only the Federal Government can regulate, and so forth, but I do think that there has to be some way to verify at the Federal level that those specific programs have—are being given support and funds are being utilized. I don't think it in any way violates the concept of the block grant.

HEALTH EDUCATION

Let me turn a moment to health education, which is one of our old issues. Dr. Foege, in your judgment, how important is the role of the school in affecting health education programs? And other community, private organizations, can they do the job as well?

Dr. FOEGE. Mr. Chairman, I start from the point of view that one of the most important jobs to be done in prevention in the 1980's, is to get people on board with the fact that they can influence their own health destiny. And that means getting a certain kind of education to them. We mentioned before, one occupational group that shows the greatest decline in smoking turns out to be physicians, and I think this is because of the kind of education they are getting now in medical school about the effects of smoking. We can hardly afford to put 200 million people through medical school in order to solve the smoking problem, but I think it gives us some idea of what can take place in the school setting.

We have been working on several curriculums over the last decade which are now being used in over 30 States, over 15,000 classrooms for about 300,000 children. The intent of the curriculum is to say you do not have to be a fatalist in this world. You can determine what happens to you within certain limits, healthwise. We think that is a very important program to support.

The kindergarten through seventh grade program is now well established, and we are evaluating it this year to see what the long-term effect is on children who have had that kind of education, what happens to the teachers who use that particular curriculum, and what happens to the parents of children who take that. We are now developing an 8th through 12th grade supplementary curriculum which is currently being tested. I think this is a very important part of prevention and public health, and one to be strongly supported.

Mr. BLOOM. In that connection, those curriculums are actually being disseminated through the National Center for Health Education, which is an organization being funded primarily with private contributions, from insurance companies, and so forth, and with the cooperation of the American Lung Association. We developed the curriculums program, tested it, and they are helping disseminate it.

I would also mention that these curriculums are part of the Department of Education's national diffusion network. It may be the only comprehensive health education curriculum that is part of that diffusion network.

Dr. FOEGE. One of the interesting things that has developed over the last year is that the Red Cross has now become involved in how to sponsor that sort of health education, health promotion message. And just as they have used volunteers around the country for CPR training, they are now looking at the possibility of training volunteers who can be used as resource people in schools, churchs, clubs, and so forth. I think we are seeing a rapid development of interest in this area.

Chairman HATFIELD. Do you have any knowledge of how many schools have the opportunity for clinical observation in hospitals in such areas, medical treatment, particularly in the area of lung cancer and other diseases related directly to use of tobacco?

Dr. FOEGE. I do not have information on how many schools use that approach. I can attempt to find it out for the record.

[The information follows:]

CLINICAL OBSERVATION OPPORTUNITIES

We are not aware of any school health education programs which actually take the children on field trips to hospitals for this kind of observation. However, one of the strengths of the school health curriculums we have developed is that they are deliberately designed to bring practicing health professionals into the classroom for slide presentations and actual demonstrations of dissection of the lungs, heart, and other organs of animals. In some schools this is done by regularly scheduled lecturers from a local hospital or health department, in others by a parent who is a physician.

APPRECIATION OF HEALTH PROBLEMS

Chairman HATFIELD. I suppose we are all products of our own environment and exposed to some degree, but growing up in the capital city of my State, the constitution required all of the State institutions to be located in that city. I think one of the very basic reasons why Oregon was an early leader in mental health was that the high schools of our State were related to the State institutions for surveys, clinical visits, mentally retarded institutions and hospitals, penitentiaries, correctional institutions, schools for the blind, for the deaf, boys' training school, girls' training school, tuberculosis hospital. All of these were located in that environ, and out of that came, I think, some very mature experiences at an early age.

People had an appreciation for some of these health problems, and where some States were still referring to insane asylums, we had come to understand the role of mental health and led in the areas of developing local mental health clinics, early removal of the stigma of mental health requirements of individual. I think there is great value in clinical experience, exposure. It seems to me that anybody who has ever stood by the bedside of a friend dying of emphysema or lung cancer related to heavy smoking, it leaves a very indelible impression.

It seems to me we get a lot of statistics—I am here speaking as a reformed smoker. I feel strongly on this matter, having lost a number of close friends, and it could have been prevented not only in lung cancer, but heart, and many others—a friend who was 38 years old had a severe heart attack and smoked heavily.

Dr. FOEGE. I absolutely agree with you, and I think that one of the tragedies of public health in this day and age is the amount of attention we expend on things of lesser importance while we are losing 1,000 people a day prematurely in this country because of cigarettes.

IMMUNIZATION

Chairman HATFIELD. Let's talk a little about immunization. Do you agree with the assertions made in the OTA report relating to the cost-effectiveness of the influence of vaccination?

Dr. FOEGE. Yes; we believe that this is a cost-effective approach. Not every year but over a period of time it is a cost-effective approach. Only 2 years ago we had 60,000 premature deaths in this country because of the influenza. We recognize that with influenza, our science is sufficiently imprecise that it is difficult to get a vaccine that is exactly what is needed each year. Nonetheless, it is clear that over a period of years, if one uses the best available, the latest influenza vaccine, that one can prevent many deaths from this disease.

HERPES

Chairman HATFIELD. Dr. Foege, we have all heard a great deal recently about herpes. A recent New York Times article reported between 5 to 20 million Americans are believed to suffer from herpes. It is contagious and I believe incurable. The article goes on and says that:

"Today that this viral infection not only has established itself as an uncontrollable epidemic, it has proved to be one of the most exacerbating ailments for patients and doctors alike."

In your professional judgment would you like to comment on the seriousness of this problem of herpes in our society, and how many estimated victims you know about, how many new cases are being reported, what the trend lines are, what progress has been made? Why is the administration proposing to reduce the funding for herpes control activities, since I believe the budget does indicate a reduction?

Dr. FOEGE. First, the question of how serious is the problem. We estimate that there are between 200,000 and 500,000 new cases each year. We estimate that there are probably at least 5 million people who currently have the virus and have periodic recurrences of it. We know that from another source of information, the number of physician visits for herpes has increased about 800 percent in 15 years, so we have every indication that it is a large problem and getting larger.

We also know it is not limited to the victims themselves, but also a problem with the newborn child of a mother with herpes. The mother does not always pass on herpes, not even when she is having a recurrence. But about 1,000 children a year are born with a herpes infection. About 500 of those children die, and about 250 of the remaining 500 will be mentally retarded. So the price for herpes is a very high one.

What can be done about it? We have seen many studies on chemotherapy. We do not know of a good way to treat it at this time. There are attempts being made to develop a vaccine, but we have no vaccine available. This means that in terms of control efforts, we do not have much to offer except for barrier controls, using condoms, and even there we do not really have good figures on the efficacy of that.

The reason that there is a reduction in our budget is simply that looking at how many dollars we had available, we had to make a decision that we could not cut back in areas where we already know how to treat the victims of venereal disease. For instance, we have about 1 million cases of pelvic inflammatory disease each year from gonorrhea, a venereal disease agent that we know how to treat. Of those 1 million cases, about one-quarter of the women are hospitalized. About 110,000 actually become sterile either surgically or because of the disease directly. About 900 of those women will die.

We had to take the position we could not cut back in efforts in gonorrhea and syphilis, where we know how to control these diseases, while with herpes we are waiting for some better control techniques before we use money for control purposes.

Chairman HATFIELD. What is the root of that philosophy? Do I understand—tell me again how many new cases per year you estimate are becoming victimized by herpes?

Dr. FOEGE. We estimate 200,000 to 500,000 per year, and that is on a base of about 5 million people who already have had the disease and have recurrences.

Chairman HATFIELD. 200,000 to 500,000 per year? And you are treating how many in the area of known control and known therapy? You said about 1 million?

Dr. FOEGE. First, with venereal diseases in general, if we lump them together we estimate there are probably 10 million new cases a year. Of that number, we have 1 million cases of gonorrhea reported. We expect that means that there about 2 million, because our study shows that surveillance reporting is about 50 percent effective. We believe that there are about 2 to 3 million clymidial infections. The 5 million cases of gonorrhea and clymidial infections result in about 1 million women acquiring disease beyond just the venereal disease as we usually know it. For instance, venereal disease can lead to pelvic inflammatory disease where the tubes, the ovaries, the uterus actually become inflamed. Of those 1 million women with pelvic inflammatory disease, about one-quarter of 1 million are hospitalized with the illness.

Chairman HATFIELD. It is like having a finger on one part of the dike and then spouting water out of the other part of the dike.

Dr. FOEGE. While the decrease in venereal disease is heartening, we now have penicillin-resistant gonorrhea in this country. The first cases came as recently as March 1976, and we have put extra attention on penicillin-resistant cases trying to break the transmission. But we have had over 4,000 cases since then, and over half of those last year, so that we are not staying ahead of even the penicillin-resistant problem.

This past year we isolated a strain of gonorrhea that is resistant to both penicillin and the alternate drug which has been used, spectinomycin. So you are exactly right. As we start controlling one problem, we end up with other problems to deal with. It is never-ending.

Chairman HATFIELD. How does the MX missile help in solving this problem?

Dr. FOEGE. I have not found a connection.

Chairman HATFIELD. This is again one of those examples where this narrowly defined issue of national security, where it is only looked upon in terms of megatons or hardware, is missing some of our real problems of national security vis-a-vis adequate education, nutrition, housing, infrastructure of the Nation vis-a-vis transportation, and so forth, and the underlying strength of the Nation which is the health of the people.

Perhaps we ought to transfer this to the Department of Defense and get sufficient funds for these research programs to carry on the real attack upon the security of this Nation which is the health of the people of this Nation. I am not suggesting either/or, but it does seem to me that we are again in a situation of not having, first of all, a comprehensive understanding of what constitutes national security. And, therefore, the national perspective we have had ever since the Kennedy administration, we are going to fail to deal with the real abuse of national security, the health of the people, and all these other factors.

The last President who understood national security, that was Dwight Eisenhower who happened to be a five-star general. He said there comes a time in a nation's life when additional money for bombs would lead to weakening if people are hungry, unfed, and unclothed. He demonstrated through comprehension. I cannot get it through my thick skull that somehow we have to reduce our investments here in trying to protect the health of the people, at least reduce the sources upon which we deal with that enemy. It is an enemy for the people of this Nation.

Now, we can all have the latest tank and airplane, bombers and missiles, but if we are racked with gonorrhea, syphilis, and herpes, just to name a few, you know, it is a pretty motley crew that we are defending. We are being destroyed from within. It seems to me that anything that is adding to the overall threat of the health of the people by the rate of increase that you have cited here of venereal diseases, and then to see a reduction in our preventive work, it is just not wise in terms of national security. We are not moved by the humanitarian aspects to develop the health of the people.

What is there in the lab on the herpes front? Is there any good news? Where are we researchwise? Does NIH have plenty of money for this? Are there inadequacies here in terms of the programs at NIH?

Dr. FOEGE. The hope with herpes is for a vaccine, and we are heartened by the advances of molecular biology that should make this possible. In NIH they have on the drawing board plans for a herpes vaccine. I cannot comment on the adequacy of their funding, but they are working on that and we are working with them in order to exploit this as soon as it is available.

I think what has happened in recent years on hepatitis vaccines, which did not look feasible even a decade ago, is very encouraging. It should be possible to construct vaccines for herpes.

Chairman HATFIELD. I suppose we have to reach a certain crisis over what we have today in order for people to respond. We were determined to eradicate malaria when we wanted to build the Panama Canal, down in Panama.

TUBERCULOSIS

I was delighted to read that in the past there has been a national decrease of reported cases of tuberculosis also, but recently, there is an alarmingly high incidence of the disease is evident among children.

February 3, before release of the fiscal year 1983 budget, they held a special hearing to determine whether the program is needed to control this, instead of relying on the prevention block grant in its first year of operation.

We know there is a specific budget request for TB activities. It would be useful to explore this question a bit further.

First of all, would you give me your assessment of TB as a serious health problem in this country?

Also, do you believe the block-grant prevention activities are adequate to deal with the growing TB problem among the young people, and if Congress were to appropriate funds for a separate TB program, in your professional judgment, do you believe we could do a better job of controlling the disease?

Dr. FOEGE. The first part of the question deals with how big a problem is tuberculosis. At the beginning of the century it was our No. 1 cause of premature death in this country. It has gone down to the point where last year we had about 27,700 new cases in this country.

One has to recognize that we have about 10 million people in this country who were at one time infected with tuberculosis. The vast majority of the "new cases" that we see now come from that pool of 10 million people who break down for some reason, usually because they're older people, and they have some crisis in their immune capability that causes them to break down.

But in addition to that, we have had over the last several years an influx of refugees with tuberculosis; of the 27,700, last year about 8 percent of those were in refugees.

This by itself—27,700, and the refugees—would not be cause for alarm if we have the trend continuing to decline.

The problem that I see is that we have had continuing transmission of tuberculosis in children under the age of 15, 10, and even 5, which means that it's not just a breakdown. There is transmission going on.

We calculate that about $200 million a year is spent in this country on tuberculosis; about 95 percent or more of that, in the past, has been paid by local and State funds, with less than 10 percent by the Federal Government.

At the present time, therefore, the amount of difference between the total national input into tuberculosis is not much different, whether one has a block grant or does not have a block grant.

Nonetheless, there are problems, and they are specific regional problems. It is not spread across the country; we have problems in areas where refugees are resettling, because they will have much higher breakdown rates over the next few years than nonrefugee populations.

We have problems where there are illegal aliens in this country. We have problems in almost every inner city area where transmission of tuberculosis continues, and the difficulty is: How to target special resources to those areas.

We have tried some of this by getting money from the Office of Refugee Resettlement. About $5 million this year is being put into medical screening, but most of this is for tuberculosis, in order to target funds where many refugee problems are.

We also provided some grants or contracts to specific areas—for instance, Dade County—in order to look at the Haitian-Cuban refugee problem. So there continues to be a difficulty.

In regard to the question on the block grant, the use of block-grant funds for tuberculosis control is not a new concept. In the past, tuberculosis money was put into 314(d) formula grant, which was the predecessor of the block grants. We estimate that in 1980, perhaps $10 million of 314(d) money was being spent in tuberculosis. This has continued to decline, though, because many States feel the problem has declined.

At the hearings earlier this year, I said to Senator Schmitt that the problem with tuberculosis, I think, is not one just of money; the problem is apathy. People believe this is a disease that has gone away. It is hard to reorient all of us back to the point that we recognize we still have a problem. We have to keep at it.

So it is not just a money problem, it is an apathy problem.

DISEASE REOCCURRENCE

Chairman HATFIELD. Let me ask you this: With this kind of experience on TB, does that indicate there may be other diseases that are dormant, that could reoccur under whatever given set of circumstances? Smallpox, polio, bubonic plague, that we think are no longer with us.

Dr. FOEGE. There are diseases that have disappeared, or decreased in incidence, where we have to continue surveillance programs.

Smallpox, I can say with more assurance than with almost any disease, we do not have to worry about. Smallpox virus is now limited to just a handful of laboratories around the world. Short of a real catastrophe, loosing the virus from the lab, I do not believe that we will have a problem there.

But for instance, cholera, which we had not had in this country for decades, has reappeared in the last few years, and surprised all of us, because we are continuing to have a few cases in the gulf coast.

This past year we had an outbreak of cholera on an oil rig; it constituted the largest outbreak of cholera that we have had in this country in the entire century.

We have problems with some other diseases that have developed resistance to antibiotics, that continue to be a problem. Tuberculosis is one of those. Within the last 5 years we had the first outbreak of tuberculosis in this country, in Elkhorn County, Miss., where the organism was resistant to the three main drugs used for treating tuberculosis.

This will be a problem with many diseases that have been controlled. We have to have a surveillance system to detect them if they reappear, and we have to be constantly concerned with resistance to antibiotics.

NUTRITION

Chairman HATFIELD. Let me turn to nutrition.

We have a number of nutrition programs in the Federal Government. My question really is: How does your agency relate to the Federal nutrition activities?

Dr. FOEGE. Our nutrition program is, by and large, a surveillance program, and it is limited to some very specific areas. The surveillance program tries to detect iron anemia in children, growth retardation in children, obesity in children, and problems with nutrition in the pregnancy period.

We have recently published a paper on the effect of low birth weights and infant mortality. For years we have been hearing how the United States is 13th, 15th, or 17th on the list of infant mortality for industrialized countries.

Our people have used this to indicate that our health care system is inadequate. We have recently done a study with Scandinavian countries to show that at any given birth weight, our infant mortality is no higher than in the Scandinavian countries.

Our real problem with infant mortality turns out to be that we have too many low birth weight babies, and this in turn can be related directly to the nutrition of the mother during pregnancy, and that is related to poverty, so that our infant mortality problem in this country has a very direct link to poverty.

But in answer to your question, our nutrition program is based on surveillance of trying to detect problems, rather than providing food supplements, and in evaluating the effect of the other programs.

TRANSFER OF NIOSH

Chairman **HATFIELD**. The political question on the transfer of NIOSH. Last year the President requested Congress to approve the transfer from Rockville, Md., to Atlanta, Ga. As you recall, Congress made a political decision to include language which prohibited the use of funds.

What is the status of that issue? The proposed move of NIOSH?

Dr. **FOEGE**. First, Mr. Chairman, let me indicate that I take full responsibility for the recommendation that the move take place. I have been concerned for some years by the fact that there has grown a separation between occupational health and other areas of public health. It has occurred to me that that should not take place, because it does not matter whether a person has lead intoxication because of occupational exposure or because they live downstream from a smelter, or because a child eats paint chips. The problem is still the same—of lead intoxication, and there has to be a program for detecting such people and getting them treatment.

I was of the opinion that our occupational health program could become stronger if the leadership would be in the same place where we have our environmental health leadership, because they're often dealing with the same problem—one in the workplace, one outside of the workplace.

I also thought that we could strengthen occupational health if we used more of our epidemiologists and our epidemiological techniques; and if we used the surveillance systems and the prevention systems that already exist at State and local health departments. Because of this I made the recommendations to the Secretary.

I was also concerned about the scientific work in NIOSH, because people were telling me that there were questions about the scientific credibility of the work. We had several incidents where the scientific recommendations came into question. We had to have outside groups look at the facts, and advise us on whether the recommendations were good or not.

I was also concerned by the fact that we had duplicative administrative functions; that we had information people, procurement and contract people, in both Rockville and in Atlanta. We calculated that we could save $1.5 million a year by moving the headquarters from Rockville to Atlanta. That money could then be taken out of administration and put into the scientific aspects of NIOSH.

It was on the basis of these reasons that I recommended to Secretary Schweiker that the move be made. The move had been started, and we had the Director, the Deputy Director, some of the top NIOSH management people, in Atlanta at the time that the congressional resolution said we could not spend money on the move.

We have continued in this position of having some people in Atlanta and some people in Rockville. We prepared an explanation of our reasons for the move, and with your permission, I would like to enter it into the record, and would be willing to then respond to other questions.

We are in the middle of the transfer. We are hoping that this restriction will be lifted, so that we can complete the move and get on with the important work. We think that even in occupational health there are some problems we should be able to eradicate—asbestos exposure in occupational settings, the lead exposure in occupational settings, certain injuries—and we would like to be able to get on with that.

Chairman HATFIELD. What is the basis for the opposition?

Dr. FOEGE. There are a number of things. Some of them are very legitimate, as I understand them. People do not like to move, and in a time where unemployment is high, this is difficult. We have attempted to solve this by saying we help people get placed, we will try to protect everyone in Rockville so that they do not lose a job. We will do the best we can, but I doubt——

Chairman HATFIELD. There are those who do not want to move. Those who are willing, they can follow the job?

Dr. FOEGE. Those who are willing to move, they have a job.

But I think there is also a concern, quite frankly, on the part of labor, a concern on the part of Members of Congress, that this would weaken occupational health.

We do not feel that way. We are doing it because we think we can strengthen their scientific basis.

Chairman HATFIELD. Why?

Dr. FOEGE. Why are they concerned it would weaken it? I think they are concerned that this moves NIOSH one layer away from where they would like it; that is, it subsumes occupational health under the umbrella of CDC. It is already that way on paper, but there is a feeling that as long as it is in Rockville and Washington, that they can get the spotlight in a way that they can't if they are in Atlanta.

So I understand that there are real concerns, and all I can do is reassure you that the basis of my recommendation was one to strengthen the science of occupational health.

NIOSH TRAINING

Chairman HATFIELD. I note that you did not ask for any money in this budget for training at NIOSH, and you've got $5.7 million in the current fiscal year budget without a request.

Do you feel there is justification that training activities would come from the States and private sources, as stated in the budget justification? Can you defend that?

Dr. FOEGE. I think the Department has taken a position far beyond NIOSH, for the entire Department, that with a restrictive budget, that training will be one of the lesser priorities. What we see here is consistent with that departmental recommendation.

We would hope that the money that has been spent in the last 5 years—and this is a rather recent program for the educational resource centers—has developed programs at 12 universities which can continue, that they are now solid enough to continue.

The recommendation is one that goes beyond NIOSH to all parts of the Public Health Service.

CANCER

Chairman HATFIELD. Do you have any statistics on the extent of incidence of cancer directly traced to occupational exposures?

Dr. FOEGE. This is a very difficult area. Let me just give some preliminary remarks, then ask Doctor Millar, the Director of NIOSH, to expand on that.

It is clear that the majority of cancer is environmentally induced, in the sense that it comes from things we expose ourselves to in or out of the workplace. In fact, a WHO document recently stated that one-third of all cancers in the world could be prevented now, without any additional knowledge. That is a sobering statistic, because if we could eliminate one-third right now without any new knowledge, it means that these are opportunities being lost each year in prevention.

The question becomes one of how much of this cancer is self-induced, in the sense of cigarette smoking, how much of it is environmentally induced, and how much of it is induced because of occupational exposure, and what is the interaction of all three of those.

With your permission, let me ask Doctor Millar to continue on that.

Dr. MILLAR. Thank you. It is very difficult to fix a figure on what proportion of cancer deaths in the United States are due to exposures in the workplace. There have been various people who have tried to make estimates, and those estimates have ranged very widely, depending on the assumptions that they have made in reaching them.

But for purposes of discussion, the range is approximately 5 to 20 percent of all cancer deaths are attributable to the workplace. That is a wide range, and if one picks either pole, one is sure to be attacked for presenting an inaccurate picture.

I think some of the things that we do know are worth citing. For instance, in NIOSH, we maintain a very extensive computerized file of new compounds of chemicals being introduced into the workplace. We know that at present in our files there are some 3,400 chemicals which we know are either known carcinogens or known neoplastogens, which is somewhat less serious than carcinogens, and others for which we cannot say one way or the other that they are true causers of cancer.

We also find that this file is increasing at the level of about 100 to 200 new compounds each year which are known to have some relationship to the production of cancer.

I would very much like to be able to give you a clear, comprehensive, and concise figure, but because of difficulties in surveillance, we do not have a national reporting system which really gets at this in a way that we get at, for instance, diphtheria or other diseases of that sort.

I would like to be able to give you the figure, but I think if one assumes that it is somewhere between 5 and 20 percent, that that is a reasonable approach.

HOSPITAL INFECTIONS

Chairman **Hatfield**. How serious is the problem of morbidity and mortality resulting from contracting of hospital infection? And to what extent do hospitals use their own resources for treating the infections?

Dr. **Foege**. Again, this is a problem where our modern techniques cause a paradox of improving things on the one hand and making them worse on the other.

As we get new, invasive techniques in the hospital, we have more problems with infection. We estimate at the present time we have about 2 million persons developing an infection in the hospital that they did not have when they entered the hospital, which is about 5 percent of all patients entering hospitals.

For each one of these patients, we estimate that it adds about 4 days, approximately $700 to their hospital bill, so it means hospital infections cost us over $1 billion and probably closer to $1.5 billion a year.

We are just completing some studies that show that hospitals are improving the problem considerably, that the techniques that have been added in the last decade to control hospital infections are, in fact, having an impact.

We expect that between 15 and 20 percent of hospital infections can be prevented with the current procedures.

There are 20,000 direct deaths and 60,000 indirect deaths because of infections in the hospital. Most of the control money is not coming from local sources; that is, the hospital builds this into their own plan.

Most hospitals have an infection control person responsible for surveillance in the hospital and coming up with control techniques.

We recently had meetings with not only State health officers, but with deans of schools of public health, and teachers of preventive medicine. As part of this we have had a committee look at what is the first problem that we should look at as a group, to come up with a curriculum that can be used in schools of public health, could be used in medical schools, could be used by State health departments.

The decision was made to use hospital infections as our first problem. A curriculum has been developed, it has been recently tested, and it appears that this will be a collaborative effort between States, schools, and the Federal Government.

Chairman **Hatfield**. Dr. Foege, gentlemen, you have been very responsive, and presented very excellent testimony.

SUBMITTED QUESTIONS

We appreciate your efforts very much and we encourage you in your efforts. Additional questions will be submitted to you for response in the record.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

TRANSFER OF ADMINISTRATION OF BLOCK GRANTS

Question: For FY 1983, the Administration proposes to place the administrative responsibility for the Preventive Health and Health Services Block Grant in the Office of the Assistant Secretary for Health (OASH) instead of in the Centers for Disease Control. How much would this transfer actually save in administrative costs?

Answer: The primary benefits of this proposal are to streamline Federal administrative functions regarding the grants and to simplify State administrative functions by providing a single PHS contact point. Although savings through this more efficient approach are expected, no estimate of the amounts involved has been developed. A comparison between administrative costs of the categorical grants with the Block Grants can serve as an example of the administrative cost savings in consolidation. In FY 1983 the Public Health Service is requesting a total of 80 positions for administration of the four PHS block grants. This represents approximately 5.4 percent of the total number of positions formerly used in the Public Health Service administering the categorical programs consolidated into the block grants.

HEALTH EDUCATION

Question: The FY 1982 Labor-HHS-Education Appropriations report directed the Department of HHS to see that there is full participation of educators in school health education programs. This Committee remains deeply committed to the area of health education as a cost-effective means of disease prevention and views the role of the school as an important vehicle to carry out this mission. To what extent are school health education personnel involved in health education programs?

Answer: Relatively few of the 17,000 school districts throughout the country have formally trained School Health Educators. Nevertheless, many school health education personnel are, or have been very much involved in health education activities at CDC, such as program and technical services related to school curriculum development, training and support of school personnel, and development of teaching and learning resources for use in classroom settings.

Local classroom teachers and school administrators who are not health educators have been involved in CDC's School Health Curriculum Project and Primary Grades Health Curriculum Projects. The success of these 2 projects is due largely to intensive participation by these main stream educators, who have received short-term training in health. These CDC developed curricula are now is use in 10,000 classrooms, reaching 300,000 children per year.

College and university based school health educators are involved in a wide variety of CDC health education activities in other than school settings, such as risk reduction programs, patient education, immunization and venereal disease.

Question: What types of health education activities are States conducting with their federal preventive health block grant funds?

Answer: Since categorical funding under the 1981 Health Education-Risk Reduction grant supports State programs until August 1982, relatively little block grant funding has thus far been used for health education purposes. This program currently exists in all States and provides the capacity to develop and manage State and local activities for the following health risk factors: smoking and alcohol abuse, obesity and nutrition problems, lack of exercise, stress, hypertension, and accidents. It also supports local education activities to deter children and youth from smoking and alcohol abuse in 130 communities.

Some States are planning to use block grant funds to continue effective smoking and alcohol education programs for youth. Some States are planning to provide "seed money" to local health and education agencies and organizations for start-up activities aimed at specific target populations, as well as to support on-going activities at the State level.

Question: To what extent are health education programs taking a back seat to more pressing health services as they compete for limited block grant dollars?

Answer: CDC considers health education/health promotion programs to be one of the most pressing needs in public health today. Through these programs, informed individuals will be able to make choices to change their behavior, rather than having to resort to more expensive alternatives to repair chronic health conditions.

The States have not had to make final decisions yet about currently funded programs because the CDC Health Education/Risk Reduction grants do not terminate until August, 1982. Some State programs have indicated concern because of the difficult competition for limited funds available.

RISK REDUCTION/HEALTH EDUCATION

Question: Risk Reduction and Health Education funds were folded into the Preventive Health and Health Services Block Grant which is in its first year of operation. Your FY 1983 budget requests $1.3 million for Risk Reduction and Health Education activities separate from the block grant. For what specific health areas and activities will these funds be used?

Answer: Although CDC uses a comprehensive approach in dealing with multiple risk factors of personal behavior which impact on the public health, activities will emphasize four (4) important areas in which Risk Reduction-Health Education funds are to be used for research and for providing assistance to States for health promotion technology:

1. Health Risk Appraisal, a new, rapidly developing approach to assess health risk status;

2. School Health Education, a key to health promotion, since it becomes harder to reduce risk once personal behavior has become ingrained in adulthood;

3. Improved Health Education Evaluation, a key component to answer critical questions which program managers are often unable to answer; and,

4. Surveillance and Epidemiology, key elements in assessing the levels of and the probable cause and consequence of risk factors.

Question: Is $1.3 million adequate to support these ambitious goals?

Answer: Yes. These funds will allow us to retain a core competence in these areas, and we will be able to provide appropriate response to States requesting technical assistance and consultation on the health education and risk reduction activities they carry out under the block grant.

Question: By requesting these funds, are you saying that this is an area of such importance that the Federal government should maintain a separate interest beyond the States' own program funded out of the Block Grant?

Answer: The Preventive Health and Health Services Block Grant turns the primary funding role for these health promotion programs over to the States. CDC is working closely with States who request assistance and consultation on effective ways to improve and to evaluate the impact of health education programs. Most States do not wish to maintain technical expertise in all areas of health promotion, especially when it may only be needed at certain points in the life of their programs. CDC can provide this assistance more cost-effectively at the Federal level than would be the case if each State duplicated technical skills. In addition the States can improve ongoing programs supported by the block grant funds from the results of research and evaluation findings conducted by CDC. Thus, they can allocate more of these funds to direct support of health education-risk reduction activities.

CHILDHOOD IMMUNIZATION

Question: What are your specific goals for the coming year in the childhood immunization programs?

Answer: Our major goals for vaccine preventable diseases in 1983 are to continue efforts to eliminate measles cases in the United States other than those which are imported or related to imported cases, and to see a continuing downward trend in rubella, mumps, pertussis, and tetanus, all of which reached all-time lows in 1981. Our major operational goals are: (1) To maintain immunization levels for all children under the age of 15 above 90 percent against measles, polio, diphtheria, tetanus, and rubella, and to raise or maintain immunization levels for children under age 7 above 90 percent against mumps and pertussis, as well as measles, rubella, polio, diphtheria, and tetanus; (2) to develop, test, and implement systems for use in the States to ensure that 90 percent or more of all children complete basic immunizations which will prevent the development of large numbers of susceptible children and adults in the future; (3) to ensure that the supply of childhood vaccine is not interrupted; and (4) to continue to expand our knowledge concerning the safety, efficacy and appropriate use of new and existing vaccines.

Question: Will more or fewer children be immunized in fiscal year 1982 compared with fiscal year 1981? Will the FY 1983 budget increase or decrease the number of children immunized?

Answer: Historically, funds available through the immunization grant program have supported the purchase of about half of the childhood vaccine purchased by the public sector. In 1981, 28 million doses of vaccine were administered in the public sector. Approximately 43 percent, or 12 million, of these were purchased with immunization grant funds. Approximately 4.6 million children were immunized with the 12 million doses of grant-purchased vaccine. We estimate that 27 million doses of vaccine are needed in the public sector in 1982, and that 24 million will be needed in 1983. It is projected that immunization grant funds will allow the purchase of some 10-11 million doses of vaccine in 1982 and 9-10 million doses in 1983, assuming a vaccine cost increase of 10 percent in 1983. We project that between 3.8 and 4.2 million children in 1982 and between 3.4 and 3.8 million children in 1983 can be immunized with vaccine purchased with immunization grant funds.

The need for immunizations have decreased in the past four years because: the backlog of unimmunized children has decreased greatly; all 50 States now have immunization requirements for school entry; 39 States have immunization requirements for all students from kindergarten to twelfth grade; voluntary groups are involved as never before; and there has been a significant improvement in parental knowledge of immunization benefits.

Any shortfall in vaccine can be obtained with State and local resources or with other Federal funds, such as the Maternal and Child Health and Preventive Health and Health Services block grants. Even before these flexible block grant programs were enacted, other Federal grant funds have been used by States to purchase vaccine.

Immunization

Question: A recent Office of Technology Assessment (OTA) report entiled "Cost Effectiveness of Influenza Vaccination" reported that "Without strong federal support, the use of influenza vaccine remains at a level too low for society to fully reap the potential benefits". OTA also remarks that at present, the federal government spends little effort to promote the use of influenza vaccine. Are you familiar with this OTA report?

Answer: CDC staff are familiar with the OTA report. The Centers' staff provided information to the OTA on various occasions during the development of the report on cost effectiveness of influenza vaccine, and received draft and final copies of the Report.

Question: How can we do a better job of vaccinating high risk populations, such as the elderly and those with pre-existing illnesses, against influenza?

Answer: Vaccine recommendations for high risk groups have been made annually for nearly 20 years. Each year, the current recommendations are distributed to nearly 90,000 individuals, institutions, and health-care groups through CDC's Morbidity and Mortality Weekly Report. Various medical societies endorse and disseminate these recommendations through their journals, newsletters, and seminars. Four drug companies produce and promote influenza vaccines each year to thousands of physicians. To substantially increase acceptance of the vaccine beyond its current distribution of about one million doses annually would require a special intensive immunization effort by States and local health departments which could cause a delay or postponement of other health priorities.

HERPES

Question: A subject we've heard quite a bit about lately is herpes. A recent New York Times article reported that between five and twenty million Americans are believed to suffer from herpes, a highly contagious, recurrent and incurable condition. The article goes on to report that "Today, this viral infection has not only established itself as an uncontrollable epidemic; it has proved to be one of the most exasperating ailments, for patients and doctors alike." Has any progress been made in developing a treatment for herpes?

Answer: Although no adequate treatment exists, some progress has been made in treating certain infections of newborns. The drug, adenine arabenoside, has demonstrated effectiveness in treating newborns with either disseminated herpes disease or localized brain infection. Another promising antiviral drug is acyclovir, which is very specific for herpes viruses. Used topically in a 5 percent ointment to treat genital herpes, it reduced viral shedding although its effect on the clinical symptoms of the disease was not dramatic. Further tests are being conducted to evaluate its effectiveness when applied topically and when given orally.

Question: What hope is there for herpes sufferers?

Answer: With the current level of medical interest and intensified research on this very complex virus, I feel we have every reason to hope that an effective drug and/or vaccine will be available in the not-to-distant future.

Question: To what extent is the NIH involved in research leading to possible treatment and a cure for herpes?

Answer: NIH supported research is studying the genetic material of this very complex virus. These studies, together with the knowledge of specific genes, are important to the eventual design of new attenuated HSV that can be considered safe for live vaccines and for targeting of antiviral compounds for treating herpes infections.

Question: How much are you proposing to cut?

Answer: A total of $1.7 million is proposed to be cut from the CDC direct operations budget for STD activities for Fiscal Year 1983. About one-half of this amount is related to herpes studies.

Question: What activities would be eliminated?

Answer: This cut in resources will cause a reduction in ongoing and planned herpes activities including the implementation of a national surveillance system for congenital herpes, studies designed to evaluate the transmission of herpes among sexual partners, evaluation of preventive educational strategies for herpes, and collaboration with NIH multi-centered projects.

FLUORIDATION

Question: The Washington Post reported in January that tooth decay has been reduced by "an astounding one-third in American children in the past decade" and that is directly attributable to fluoridated water supplies and fluoride in toothpaste. It also stated that 59% of American children between the ages of 5 and 11 had never had a cavity, according to the latest survey of the National Institute for Dental Research. Now that it is included in the block grant, how will the fluoridation program fare?

Answer: Each State has flexibility under the Preventive Health and Health Services Block Grant to decide which preventive health programs they will continue, and the level of block grant funding which they will allocate to those programs. Project funding periods for categorical fluoridation grants actually extend into the current fiscal year, so it has not yet become clear what funding priority the States will assign to the program once the categorical funding has terminated.

Question: Have any States significantly reduced or eliminated their fluoridation activities?

Answer: Three States (Connecticut, Michigan, and New Jersey), that previously received categorical fluoridation grant funds, have indicated to the Centers for Disease Control that they will not continue to support fluoridation activities after the categorical funding periods end. The level of support the fluoridation program will receive in the other States is unknown at the present time.

Question: Do you believe there is a need for continued Federal technical assistance in the area of fluoridation to continue to assist the States in developing their own programs?

Answer: For the past several years, the Centers for Disease Control (CDC) has provided direct technical assistance and consultation, when requested, to States and local communities to plan for and initiate community fluoridation programs. Assistance has also been provided in all engineering phases of fluoridation as well as in the development of monitoring/surveillance programs to ensure the maintenance of the optimal level of fluoride. Additionally, training programs for State health personnel have been provided which have developed their capacities to plan, initiate, and operate fluoridation programs. It is expected that as a result of this extensive technical assistance and the experience gained, State and local communities will apply this knowledge to plan and manage their respective fluoridation programs. Although no specific resources are requested for this purpose in 1983, the CDC will continue to provide technical assistance when requested, to the extent that resources permit.

TUBERCULOSIS CONTROL
TB AND REFUGEES

Question: We continue to hear expressions of concern about the general health of refugees entering the U.S. Are health screening and treatment requirements being followed in overseas staging areas and in the U.S.?

Answer: Yes. Health screening and treatment of Indochinese refugees in overseas staging areas is performed by the Intergovernmental Committee for Migration (ICM) under contract with the Department of State. Oversight is maintained by CDC personnel stationed in Bangkok, Thailand. Current policies and procedures are being followed and will continue to protect effectively the health of refugees and safeguard the health of the American public. Similar screening and treatment programs are carried out for all immigrants, including refugees coming from other parts of the world.

Question: Are the health assessment requirements for admitting refugees adequate to protect the public health?

Answer: The various agencies closely involved with the health screening of refugees are convinced that present screening procedures and requirements are adequate to protect the public health. Since October 1979, approximately 300,000 Indochinese refugees have been screened for health conditions before leaving refugee staging areas in Southeast Asia.

CDC also coordinates a domestic health assessment program which is intended to include all Indochinese refugees soon after their arrival in the United States. This program not only addresses the health conditions of public health concern, but also includes other conditions which can be an impediment to the effective resettlement of refugees. Refugees found with any of these health problems are treated or referred for treatment by State and local health departments.

Question: How reliable are management information systems for assuring that refugees are screened, tracked, and treated as intended?

Answer: An excellent medical record documentation system was put in place at the beginning of the overseas screening program. ICM prepares the refugee's medical folder which accompanies the refugee to the United States including an x-ray for tuberculosis, a record of the physical examination received (four copies), and an immunization form clearly identifying the vaccines received and those immunizations which need to be completed. State and local health departments receive notification of all arrivals by mail, copies of appropriate medical documents, and receive telephone calls within 24 hours from the ports of entry if a refugee has a medical condition which needs prompt followup in the refugee's area of initial resettlement. CDC then closely monitors the followup of these cases. To date, CDC records show that over 90 percent of these cases have been seen, evaluated, and treated, if necessary.

ENVIRONMENTAL HAZARDS

Question: Increasingly, we seem to be succeeding in controlling catastrophic epidemics due to sophisticated medicine and technologies. Do you believe therefore we should be able to turn our attention to health problems relating to environmentally related diseases such as exposure to low levels of harmful substances?

Answer: Although we have been able to prevent or control many infectious and deficiency diseases by use of replacement therapy, drugs and immunizations, we still face major problems such as drug resistence and the discovery of new organisms and new opportunities for prevention as vaccines and other new tools are developed. The major effort in the next decades will be to maintain, at least, that level of health; to expand our knowledge and efforts about what people can do for themselves healthwise and begin to extend our efforts in chronic and environmentally related diseases. These efforts include research, prevention, control and therapy of conditions arising from both high and low exposures to harmful substances. Each age beginning with intrauterine life and extending into old age has its own set of potentially harmful exposures. The exposures result from lifestyle choices, occupation and the general living environment. Even though scientists are capable of measuring smaller and smaller amounts of potentially harmful substances, it may be that health effects can only be adequately defined for the more highly exposed populations. Nevertheless, when documented and measured exposures even at low levels occur in populations of adequate size, they should be considered for long term study.

Question: What are some examples of projects that CDC will undertake in FY 1983 relating to low level exposure problems?

Answer: CDC (often in collaboration with state health departments) will continue to follow the populations with low level chemical exposures in Michigan (PBB), Alabama (DDT), Arizona (asbestos), Massachusetts (PCB, mixed), New York (mixed) and Kentucky (PCP). In addition, we will continue to follow populations 1) of nuclear test participants, 2) living around Three Mile Island and 3) owning gold rings with low level radiation exposure.

Question: How serious is the health problem relating to asbestos exposure?

Answer: Asbestos fibers are ubiquitous in the environment and virtually all persons are exposed to a greater or lesser extent. Such exposure is a major problem for persons engaged in industrial use especially if those persons are cigarette smokers. This combination of asbestos exposure and cigarette smoking is particularly hazardous leading to a markedly increased risk for lung cancer among persons so exposed.

Human occupational exposures to all commercial asbestos fiber types, both individually and in various combinations have been associated with high rates of asbestosis, lung cancer, and mesothelioma. While significant excesses of cancer of several other sites have been observed in exposed workers, presently available information is insufficient to determine the role of specific fiber types.

Available data show that the lower the exposure, the lower the risk of developing asbestosis and cancer. Excessive cancer risks, however, have been demonstrated at all fiber concentrations studied to date. Evaluation of all available human data provides no evidence for a threshold or for a "safe" level of asbestos exposure.

Workers are not the only persons experiencing asbestos-related disease. Household members of asbestos workers and individuals living near asbestos sources have experienced excess deaths due to asbestos-related disease.

From 1940 through 1979, 13,200,000 individuals had significant potential exposure at work. 9,200,000 are estimated to be alive as of January 1, 1980. Currently, it is estimated that 8,500 asbestos-related excess cancer deaths occur annually in the United States. This is expected to rise to about 10,000 deaths annually until 1990. This phenomena is due to the long latent periods associated with asbestos-induced diseases (usually 15-40 years after initial exposure). It is expected that after 1990 the mortality rate of 10,000 deaths annually will decrease but will remain significant over the next three decades. This decrease is a result primarily of increased awareness of asbestos-related hazards and associated diseases as well as regulatory activities.

Question: Does CDC have any plans in FY 1983 to address this problem?

Answer: Our Center for Environmental Health is currently working with the Arizona State Health Department about human exposures to asbestos mill tailings in Globe, Arizona. This effort will continue into 1983. Also, NIOSH will continue its morbidity and mortality study of railroad workers exposed to asbestos. It is believed that this group of workers represent a unique exposure to one type of asbestos, chrysotile. The Institute is also developing a criteria document to be transmitted to the Department of Labor on asbestos exposures in mining. We will continue to address unique exposures to asbestos through NIOSH's surveillance and health hazard evaluation programs.

Question. What efforts has CDC made alone or in coordination with other agencies, in controlling human exposure to Radiation, both ionizing and non-ionizing?

Answer. CDC works with Food and Drug Administration (Bureau of Radiological Health), Nuclear Regulatory Commission, Federal Emergency Management Agency and other Federal agencies concerned with radiation control to respond promptly to potential health threats from radiation accidents (nuclear power plant releases, nuclear waste spills, etc.). CDC assumed the lead HHS role in this respect at the time of the Three Mile Island episode. CDC also carries out field investigations in cooperation with State and local agencies when particular radiation exposure problems arise. Recent examples have included evaluation of human exposures in connection with a uranium mine waste spill in Church Rock, Arizona, and evaluation of possible increases in cancer near nuclear facilities in Maine and Tennessee.

SUPERFUND

Question: CDC is responsible for implementing health activities of the so called "Superfund", which has been established to provide a broad-based federal capability to address the problem of hazardous wastes in the environment.

EPA receives the actual appropriation and decides how much of it should go to the other Departments for their areas of responsibility. What specific health activities will CDC conduct as part of the Superfund effort?

Answer: CDC will serve as HHS lead agency to coordinate the implementation of the various health components defined under "Superfund". Based upon EPA's projected workload, we anticipate providing health consultation and assistance for 1,500 site inspections, with HHS staff on-scene consultation for the 300 planned EPA site investigations. Emergency health-related field support and assistance will also be provided for an estimated 125 spills and at 28 other immediate removal Superfund sites. Guidelines and protocols for health studies, investigations, and disease registries will be developed and consultation services will be provided to EPA on development and/or monitoring of worker safety plans on a site specific basis. Assistance will be provided to EPA in development of Superfund guidance material to assure appropriate consideration is given to public health issues. Short term toxicological testing will be conducted for chemicals and chemical combinations for which there is little or no information. This information and other data will be used as we augment the

Toxicological Data Base so that the most advanced information will be available as the public health concerns are addressed at Superfund sites.

Question: How much have you requested from EPA for that purpose in FY 1982? FY 1983?

Answer: HHS requested $10 million for FY 1982 and $20 million for FY 1983 for health activities under Superfund.

Question: How much is EPA willing to provide?

Answer: At this time, EPA is planning to transfer $3.344 million to HHS for FY 1982 and $3.217 million for FY 1983. We plan to negotiate for additional funds for health studies and toxicological testing on a site specific basis.

NUTRITION SURVEILLANCE AND MONITORING

Question: What are the goals of CDC's Nutrition Surveillance Program?

Answer: The goals of CDC's nutrition surveillance program are to provide increased technical assistance and consultation to States to aid them in developing, implementing, and managing effective nutritional status surveillance as an integral aspect of their service delivery programs. Technical assistance and training will be furnished, in collaboration with the Health Education Division, to states and other agencies in the management, objective setting, and assessment of risk reduction programs intended to reduce chronic diseases associated with nutritional and other risk factors, especially among high-risk populations. Though efforts are now directed towards the pediatric and pregnant populations, development of an effective means to assess and monitor the nutritional status of the elderly will continue, and assistance will be provided to examine appropriate surveillance indices for other high risk groups.

Efforts will be made to improve the quality and use of uniform and correct procedures for nutrition assessment, and additional anthropometric, biomedical, and clinical measures will be identified, developed, and validated for use as inexpensive and sensitive screening tools.

CDC plans to enlarge its epidemiologic activities to include investigations regarding health implications of nutritional status indices and the identification and validation of specific nutritional status indices for use in different situations.

Question: Based upon nutrition information gathered by CDC and other Federal programs over the past few years, what general conclusions can we now draw about the relationship between diet and health?

Answer: There are health problems associated with undernutrition in isolated cases. Iron deficiency anemia is the most prevalent of these problems. However, our information indicates that overnutrition is by far the more prevalent nutritional problem. We find excessive proportions of high weight-for-height (i.e., children who weigh more than the growth norms for their height) in many different populations for which we have surveillance data.

Infant mortality in this country has a direct link to poverty. We have too many low birth-weight babies which can be related directly to the nutrition of the mother during pregnancy which is related to poverty.

TRANSFER OF NIOSH HEADQUARTERS

Question: Last year, the President requested that Congress approve the transfer of headquarters employees of the National Institute of Occupational Safety and Health from Rockville, Maryland to Atlanta, Georgia and Cincinnati, Ohio. The Congress, however, included language on the Continuing Resolution which prohibited the use of funds in that bill for such a move. What are the primary reasons for such a move? How much is the expected savings over the next few years, should such a move take place? How many individuals would be affected by this transfer?

THE NIOSH MOVE

Background

Public health and occupational safety and health share common roots and basic skills--epidemiology, engineering, medicine, environmental hygiene, chemistry, toxicology, and health education. However, the evolution of occupational safety and health, especially in recent years, has diverged markedly from the rest of public health. Understanding this divergence is essential to understanding the origins of the present conflict surrounding the move of NIOSH headquarters.

American public health has its roots in 18th Century attempts to control epidemics. It reflects the evolution of the distribution of powers between the States and Federal government set forth in the American Constitution. Local boards of health and later State health departments sprang up to do what clinical medicine could not do--provide common protection to citizens against a common threat through prevention. The subsequent evolution of public health established a principal operational role for local health departments, and acknowledged the ultimate responsibility of the States for disease control. The federal role which evolved was one of assisting the State and local health agencies with expertise, people, and money when requested. Medical practitioners and voluntary health organizations played important and sometimes crucial adjunctive roles in the practice of public health.

Indeed, public health is generally viewed as serving the community's general needs within the limits of resources. While these roles and relationships were forged around issues of communicable disease control, the patterns established are being reinforced in maternal and child health, environmental health, chronic disease control, and more recently in programs of health promotion. In the public health sphere, CDC is generally viewed as the federal agency most closely associated with the practice of public health, most clearly in the mainstream of American public health and most responsive to state public health needs and programs.

Occupational safety and health had a far different beginning. It began as a surgical service for treating those wounded in factories. With the advent of workers' compensation, a type of preventive medical measure was introduced in the form of the pre-employment physical exam. To contain the costs of curative and compensation services, companies brought in industrial hygienists and engineers to attempt to reduce dangerous exposures. Initially these preventive skills were drawn from outside the company, notably from local and State health departments. However, the major companies soon developed their own in-house industrial hygiene and safety programs. With the emergence of collective bargaining, occupational safety and health became a bargaining issue, and inevitably was considered as a benefit to workers under contract, rather than an expected community service from the health department.

Over the years, most American workers have been in jobs which are not unionized and in businesses without industrial health programs; they were only indirectly affected by these developments. In 1936, in an attempt to broaden the availability of technical expertise, assistance and advice, the U.S. Public Health Service conducted a program to establish industrial health units in each State health department. In 1964, 41 States plus the District of Columbia and Puerto Rico, had active industrial health units and all but four were located in State health departments. In addition, there were 36 such units in city or county health departments. They varied considerably but typically included industrial hygienists, chemists, engineers, physicists as well as physicians and nurses. These programs emphasized training and service, rather than regulation and enforcement and made specific attempts to assist small businesses.

Advent of the Occupational Safety and Health Act (OSH Act)

Advocates for better working conditions were unimpressed with the efforts of State health departments. They argued that regulation of industry was needed to solve worker health problems, and saw the Federal government as the logical central focus for such regulations. In 1970, the Occupational Safety and Health Act (OSH Act) was enacted which fixed central responsibility for worker health in a Federal agency located in the Department of Labor (Occupational Safety and Health Administration (OSHA) for general industry, and later the Mine Safety Health Administration (MSHA) for mining).

The Creation of NIOSH

The OSH Act stopped short of a complete divorce between occupational safety and health, and public health at the Federal level. It created, in the Department of Health, Education, and Welfare (HEW), a National Institute for Occupational Safety and

Health (NIOSH). CDC believes that this placement was to assure that the Institute would remain an objective scientific organization dedicated to improving worker health and safety.

The name National Institute implies a commitment to impartial science and objective interpretation. These concepts are not always consistent with single-purpose advocacy.

On June 23, 1981, the Assistant Secretary for Health, Dr. Brandt, announced the decision to relocate the NIOSH headquarters from Rockville, Maryland, to Atlanta, Georgia, and at the same time to transfer the standards development functions to Cincinnati, Ohio. A new Director, Dr. J. Donald Millar, was appointed with his duty station at the new headquarters in Atlanta, Georgia.

A few key staff vacancies were filled in Atlanta, with the completion of the transfer scheduled for November 1, 1981. During the summer, there were long and intensive negotiations with AFGE Local 41, the employee organization with exclusive recognition for representing NIOSH employees in Rockville. There were Congressional hearings. The House of Representatives and then the Senate (by the time of the third Continuing Resolution) passed amendments to the Appropriation Acts which prohibited the expenditure of funds in fiscal year 1982 for the purpose of moving NIOSH headquarters or any staff from Rockville to Atlanta or Cincinnati.

The effect of that Congressional action was to interrupt the transfers. NIOSH has been operating with its headquarters--its Director, Deputy Director, Executive Officer, and a small staff located in Atlanta with the remainder staying in Washington in ever diminishing numbers. The reduction is due primarily to employees transferring to other government positions, retirement, and voluntary attrition. In June there were 157 permanent employees in Rockville, of whom 107 were to be transferred to Atlanta and 50 to Cincinnati. As of February 6, 1982, there were 78 permanent employees still on the rolls in Rockville, with 50 slated for transfer to Atlanta, 24 to go to Cincinnati and 4 to remain in the Washington area.

Rationale

CDC's rationale for moving the NIOSH-Rockville offices was:

(1) to strengthen the scientific/technical base of the Institute

(2) to strengthen and streamline the administrative and program management functions

(3) to realize long-term cost savings

(4) to place the criteria document managers in close proximity to the Institute's research scientists

1. Strengthening The Scientific/Technical Base

The transfer of the headquarters to Atlanta assumes that in creating NIOSH, Congress intended to establish a scientific organization for service oriented research and technical assistance. It is further assumed that much of the controversy surrounding the Institute stems from the manner in which the Institute has used its scientific expertise.

The issue of the carcinogenicity of beryllium is one example of how the scientific credibility of NIOSH has been questioned. NIOSH staff produced a report indicting beryllium as a carcinogen. The strength of the evidence in the studies cited in the report was questioned. A CDC review group was established as well as an external review group. Each confirmed weaknesses in the report.

The scientific and technical base of the Institute will be strengthened by locating the headquarters of NIOSH in Atlanta, through greater interaction with the leadership and programs of the rest of CDC; greater interaction in the area of environmental health (CDC is the lead agency for responding to environmental hazards and the Department's implementation of the Superfund); increasing involvement of official health agencies in the improvement of occupational safety and health; and enhancing the Institute's surveillance efforts by closer association with CDC, which has considerable expertise in disease and health hazard surveillance.

2. Strengthening and Streamlining Administrative and Program Management

NIOSH has been a component of the Centers for Disease Control since 1973, and with its headquarters operation located in Rockville, has maintained some duplicative administrative staff capabilities. NIOSH had its own administrative and budget services, its own procurement and contracting, its own legislative/liaison staff, its own public information office, all ostensibly justified by its separation from its parent agency in Atlanta. CDC had a full set of similar services in Atlanta for the rest of its components, all headquartered in Atlanta. The result has been an over-investment in management and administration at the expense of the scientific and technical program of the Institute. The semi-independence and duplicative support functions of NIOSH in Rockville have persisted throughout the 8-year history of the relationship. As resources tightened, the costs of this duplication of functions in Rockville were viewed as an increasingly intolerable waste of resources.

In order to be able to offer employment for everyone who was willing to move, it was anticipated that any savings would have to occur over the long run (through attrition or reassignment). With the losses that have occurred since the announcement of the move, some correction of this imbalance between management and program can begin to occur immediately. The relocation to Atlanta will make it possible to consolidate certain of the administrative activities with the rest of CDC freeing NIOSH resources for program responsibility. There is an opportunity to correct an organizational arrangement that has never worked well.

An intangible but important reason for locating the headquarters in Atlanta was to obtain more direct, day-to-day interaction with CDC leadership. One of the criticisms that has been made publicly by a former NIOSH Director is that CDC did not provide enough leadership and guidance. The physical location of NIOSH headquarters with its parent agency should facilitate good management oversight by the Director of CDC and provide the NIOSH Director immediate access to the Director of CDC to assure proper attention to NIOSH needs.

3. Cost Savings

Although there would be initial costs, long term savings are anticipated. By eliminating duplicated functions now performed separately by management, administrative, and technical staff in Atlanta and Rockville, by consolidating the staff of the Division of Criteria Documentation and Standards Development with the Division of Technical Services in Cincinnati, and by streamlining the conduct of administrative functions, it is estimated that it will be possible to save approximately $1.5 million each year below what NIOSH had been allocating for these functions. For example, in the past NIOSH has allocated more than 180 permanent and more than 40 part time and temporary positions for the performance of the Rockville activities. Fewer positions will be needed in NIOSH headquarters if located in Atlanta.

4. Standards Development to Cincinnati

The transfer of staff to Cincinnati is related to a reorganization which combined the Division of Criteria Documentation and Standards Development (formerly located in Rockville) with the Division of Technical Services (formerly located in Cincinnati). This move makes good programmatic sense. The most important contacts involved in the development of scientific position statements are the contacts between the persons developing the document and the scientists responsible for related scientific work. Most of NIOSH's research scientists are in Cincinnati; the rest are in Morgantown. To get the best scientific base for recommendations, it is more important that the document managers now assigned in Rockville be in daily contact with the Institute's research scientists rather than with special interest groups in the Washington area.

Correcting Misconceptions

Constructive review of the decision to transfer activities to Atlanta and Cincinnati has been clouded by misconceptions, misstatements, unfounded allegations, and exaggerations. It is important that the record be set straight.

A. NIOSH is not being dismantled. The NIOSH reorganization approved by Secretary Schweiker and published in the Federal Register on September 8, 1981, maintains the National Institute for Occupational Safety and Health as one of the major program components of the Centers for Disease Control--as it has been since 1973. The move affects the NIOSH headquarters activities (program management and administration) in Rockville by moving them to Atlanta; the Cincinnati operations by augmenting them through the addition of the standards development activities, and does not affect the Morgantown laboratories. Ultimately, both the Cincinnati and Morgantown scientific programs will benefit by the changing balance between administrative and program management and scientific and technical programs.

B. The move has not been undertaken in order to accommodate to the personal wishes of an individual. Neither the Department, nor PHS, nor CDC entertained any such proposal. The allegation maligns the present NIOSH director who has had a distinquished career in public health and is an outstanding medical officer.

C. Implementing the move will not cost $16 million. This misconception is believed to have stemmed from an assumption that a multimillion dollar construction project would have to be undertaken in Cincinnati in order to accommodate the 50 employees proposed for relocation. Actually, the transfer to Cincinnati can be accommodated within available space. It was originally estimated that if all the employees moved, the cost would be $1.8 million. If only half the employees moved, the transfer would cost $1.14 million. Attrition in the Rockville staff makes it clear that the cost of the move would be closer to the minimum of $1.14 million.

D. CDC has not engaged in unfair labor practices. Local 41 was informed of the decision to move on the same day as the Institute's management; was given reasonable notice of the transfer; and was met, in good faith, at the bargaining table. The decision to relocate an organization is management's prerogative. Management's obligation to the employees and their exclusive representative is to: (1) give them a reasonable notice of the relocation, (2) negotiate in good faith over the manner in which the transfer will take place. Both were done. Throughout the negotiations, management kept the Union informed of the deadlines involved in order to implement the scheduled move. Having given reasonable notice of the move and having attempted to negotiate in good faith, management is not obligated to delay the decision to move simply because agreement has not been reached on the details of the process.

E. CDC has not acted illegally in defiance of Congress concerning the NIOSH transfer. The headquarters had been transferred in June and steps were being taken to complete the move of personnel when the House of Representatives passed an amendment to the FY 1982 Appropriations Bill to prohibit the expenditure of funds for the transfer of the Rockville activities. That action was not binding under the first two Continuing Resolutions without similar formal action by the Senate. The Department undertook a thorough review of the legal aspects involved. As a result, from October 1 through mid-November, no permanent transfers or personnel actions were made. It was only during the brief period from November 18 until December 15, 1981, that five permanant vacancies were filled in Atlanta in order to provide the most essential resources necessary to keep NIOSH running. Once the Senate had acted and the actions of both houses had in effect been reaffirmed in the third Continuing Resolution, no further transfers of personnel or equipment were made and no additional permanent employees were hired in Cincinnati or Atlanta to carry out those activities involved in the moves.

F. The Rockville employees were not treated callously or inconsiderately. The employees were informed as soon as possible after the decision was made and given reasonable notice of when the transfer was to take place. Management set up a special outplacement program to assist those individuals who did not wish to transfer, went to considerable lengths to provide information about Atlanta and Cincinnati in order for the employees to make informed decisions, and detailed personnel specialists to Rockville in order to answer employee questions and concerns.

Conclusion

For 10 years of existence, NIOSH has been isolated from its parent agency, CDC, and from the mainstream of public health. Its scientific credibility has been questioned by critics, including former directors of the Institute.

That the current situation must be resolved is clear. The way it is resolved will greatly affect the future of NIOSH and the field of occupational safety and health. Allowing completion of the move offers hope that NIOSH will assume a proper and credible role as a respected member of the scientific and public health community.

NIOSH TRAINING

Question: In FY 1982, NIOSH training was funded at a level of $5.7 million even though there was no budget request. The Administration is requesting no funds again for training in FY 1983. Why are no training funds being requested in FY 1983?

Answer: The reducing overall reduction is consistent with the Departmentwide-policy of phasing out Federal support of established training programs for health professionals.

INFANT MORTALITY

Question: How much progress are we making nationally to reduce the overall infant mortality rate?

Answer: Nationally, the infant mortality rate has declined from 21.4 per 1,000 live born infants in 1970 to 13.1(est.) in 1980, a decline of 38.2%. This proportional rate of decline is approximately twice as fast as the decline that occurred in the 1960's. The proportional rate of decline was approximately equal by race. Thus, non-white infants continue to have an infant mortality rate that is twice the rate for white infants.

Question: How do we rank compared with other so-called "developed" nations in the rate of infant mortality?

Answer: The U.S. ranks 16th when compared with other developed nations, falling behind the nations of northern Europe. The rate among U.S. urban whites would place the U.S. approximately 7th among the developed nations, the urban non-white rate would place the U.S. approximately 22nd, similar to Greece and Italy. The rural infant mortality rates are higher than urban rates. A recent study from CDC has shown that the primary reason for the U.S. low ranking is that the U.S. low birth weight rate is considerably higher than in other developed countries.

Hospital Infections

Question: What specific activities will the FY'83 budget support in the area of hospital infections control?

Answer: The 1983 budget for hospital infections control supports activities in the following areas:

> To better understand the source and extent of hospital infection, field epidemiologic and laboratory investigations are supported especially as related to epidemics. Laboratory investigations of microbial resistance to antibiotics are supported as an adjunct to the development of recommended therapeutic regimes for controlling infections. Of critical importance in this area is the study of methicillin-resistant *Staphylococcus aureus* a frequent cause of nosocomial infections. In addition, measures to increase the application of improved control programs are supported through the development and distribution of infection control guidelines including those for employee health, hyperalimentation, pneumonia, and surgical wound infections. Finally, activities to improve the knowledge and techniques through training courses for infection control nurses and intensive care nurses are supported.

Question: To what extent do hospitals contribute their own resources to the infections control effort?

Answer: Although the CDC does not have specific data on amounts of resources devoted to infections control efforts, our experience indicates that individual hospitals support their infection control programs from their own budget.

BLOCK GRANT/PROGRAM MANAGEMENT

Question: If the Congress should disallow the transfer of the Preventive Health and Health Services Block Grant to the Office of the Assistant Secretary for Health (OASH), would you need additional program management funds to administer the block grant in CDC?

Answer: Additional program support funds and positions would be required to administer the Preventive Health and Health Services Block Grant if the Congress disallowed the transfer of this program to OASH.

Question: If so, how much would be needed for program management for this Block Grant?

Answer: Administration of the Preventive Health and Health Services Block Grant in CDC would require $1 million and 20 positions.

NIOSH RELOCATIONS

Question: Both the House and Senate bills for Fiscal Year 1982 prohibit the use of funds to move the headquarters of NIOSH to Atlanta. However, despite this clear language, several reassignments and transfers have apparently taken place since last October. What headquarters positions are now established in Atlanta?

Answer: Before the relocation of headquarters was interrupted, the Director, Deputy Director, Executive Officer, and Director of the Office of Program Planning and Evaluation were already located in Atlanta. Other employees in Atlanta provide essential staff support to these key officials. Their duties, listed on the following staffing analysis, are necessary to ensure the continuity of NIOSH programs. All authorizations for relocations were signed in September 1981 and carry an effective date of September 1981.

CENTERS FOR DISEASE CONTROL
National Institute for Occupational Safety and Health
Atlanta Staff

PRIOR TO OCTOBER 1, 1981

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Office of the Director				
Millar, J.D., M.D.	Director	Permanent	07/13/81	Directs and administers the policies and program of the National Institute for Occupational Safety and Health.
Coker, B.	Secretary	Permanent (Detail)	08/23/81	Provides secretarial and administrative support to the Director, NIOSH.
Harris, E., Ph.D.	Deputy Director	Permanent	09/06/81	Assists the Director, NIOSH, in the accomplishment of program objectives and policies for the Institute.
King, J.	Secretary	Temporary Permanent	07/22/81 10/04/81	Provides secretarial and administrative support to the Deputy Director.
Shamblee, T.	Executive Officer	Permanent	09/06/81	Assists the Director, NIOSH, in the accomplishment of program objectives through resource management and administrative service.
Morrison, B.	Secretary	Temporary Permanent	08/20/81 10/04/81	Provides secretarial and administrative support to the Executive Officer.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Office of Administrative and Management Services				
Dunkin, D.	Supervisory Program Analyst	Permanent	08/23/81	Provides program and management analysis and staff assistance to the Executive Officer, NIOSH, in areas such as budget, project planning, policy development, and personnel.
Office of Program Planning & Evaluation				
Myers, M.	Director, OPPE	Permanent	09/26/81	Directs the staff responsible for the planning of the Institute's research program and for the monitoring, control, and evaluation of that program.
Dobbin, D.	Program Analyst	Permanent	09/26/81	Provides staff support and management assistance to the Director, OPPE, in the planning and evaluation of the Institute's research program in the control of occupational hazards.
Neuhaus, E.	Clerk Typist	Temporary	09/14/81	Provides clerical assistance on word processing equipment to OPPE.
Touch, R.	Senior Program Analyst	Permanent	09/01/81	Provides staff support and management assistance to the Director, OPPE, in the planning and evaluation of the Institute's research program in identification and surveillance of occupational hazards.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
		OCTOBER 1, 1981 TO PRESENT		
Office of Administrative and Management Services				
Adams, J.	Travel Clerk	Temporary	12/28/81	Provides administrative assistance in the area of travel to the Office of the Director, NIOSH.
Beaullieu, B.	Admin. Clerk	Permanent	12/13/81	Provides administrative assistance in the areas of budget and procurement to the Office of the Director, NIOSH.
Crochet, A.	Writer/Editor	Temporary (on loan)	11/23/81	Provides editorial assistance to OAMS and the Office of the Director, NIOSH.
Foster, B.	Admin. Clerk	Permanent	11/29/81	Provides administrative assistance in the area of personnel to the Office of the Director, NIOSH.
Sumner, A.	Acting Branch Chief, Mgmt. Systems Branch	Permanent (on loan)	01/04/82	Directs the staff responsible for the Institute's management information system.
Office of Program Planning & Evaluation				
Aral, S., Ph.D.	Biostatistician	Temporary	01/24/82	Assists in planning and evaluation of the Institute's research program in identification and surveillance of occupational safety and health problems.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Darby, G.	Coding Clerk	Temporary (on loan)	11/30/81	Provides computer and clerical assistance to OPPE, NIOSH.
Groza, T.	Program Analyst	Permanent	12/13/81	Assists in the evaluation of major Institute programs and of resource administration.
Holstun, D.	Public Health Advisor	Permanent	12/13/81	Assists in the management of the Institute's program in the areas of identification and surveillance of occupational health hazards.
Medwin, H.	Clerk Typist	Temporary	10/01/81	Provides clerical support to the Director, OPPE, NIOSH.
Tozzer, N.	Writer/Editor	Temporary (on loan)	01/28/82	Provides editorial assistance to OPPE in the area of information dissemination and technology transfer.
Turenne, R.	Program Analyst	Permanent (TDY from Morgantown)	12/13/81	Provides staff support in the planning and evaluation of the Institute's program in the area of information dissemination and technology transfer.
Withers, P.	Program Analyst	Permanent	12/13/81	Assists in the planning and management of the Institute's program in the control of occupational hazards.

Question: How many employees were transferred from Rockville headquarters to Atlanta?

Answer: Three employees transferred from NIOSH/Rockville to NIOSH/Atlanta.

Two employees were recruited for position in CDC/Atlanta transferring from NIOSH/Rockville.

One employee is on detail to the Superfund Task Force in the Center for Environmental Health, CDC.

Question: Were government funds used to effect any transfers to Atlanta, and if so, how do you square the use of these funds with the express prohibitions contained in the House and Senate bills and incorporated by reference in the Continuing Resolution?

Answer: All transfers were approved before October 1, 1981, although such transfer could have legally been accomplished until December 15, 1981. All costs were obligated against FY 1981 funds except $716.42 which because of technicalities had to be charged against FY 1982 funds.

Question: Are any Rockville employees required to work part-time in Atlanta, and if so, how many?

Answer: No Rockville employees are required to work part-time regular basis in Atlanta. Several employees have, on occasion, travelled to Atlanta; this travel has been program-related and important for continuity of the Institute's program.

Question: What percent of his time does Dr. Millar spend in the Rockville facility?

Answer: From July 13, 1981, when Dr. Millar's appointment became effective, to the end of February 1982, he has spent approximately 30 days (22% of his time) in the Rockville office.

Question: How is operating efficiency enhanced by having certain headquarters personnel in Atlanta and others in Rockville?

Answer: We have not allowed administrative services to suffer in our determination to ensure the continuity of NIOSH functions. The duplicative offices functions that had been provided in Rockville have been streamlined, and a smaller number of employees are now performing the critical administrative functions of the Institute. We are automating many functions that had been performed manually, but a hindrance to this effort to improve efficiency has been a lack of equipment and staff at the Atlanta headquarters of NIOSH. We have been unable to move any equipment to Atlanta because of the ban on using appropriated funds for such purposes.

NIOSH PROJECTS

Question: What is the current status of your work regarding the occupational health hazards posed by exposure to cobalt?

Answer: In October 1981 the National Institute for Occupational Safety and Health (NIOSH) transmitted to the Occupational Safety and Health Administration (OSHA) a document entitled, "Criteria for Controlling Occupational Exposure to Cobalt." This document presents a comprehensive discussion on health effects of cobalt, the extent of exposure in work situations, occupations where exposure may be expected and presents a method for collection and analysis of airborne cobalt. In the document NIOSH makes no recommendations for changing the current OSHA environmental limit of 0.1 milligrams of cobalt in a cubic meter of air (mg/cu m), but does identify airborne concentrations at which health effects have been noted. NIOSH concludes that cobalt and all compounds containing cobalt have the potential for toxic effects on the respiratory tract, the heart, and the thyroid gland and that all are potentially sensitizing.

Based on NIOSH's assessment of existing studies on toxic effects from exposure to cobalt, serious deficiencies were found in the research concerning many cobalt compounds. This led NIOSH to conclude that additional research remains to be done before the toxic effects of those compounds can be documented. However, NIOSH also concluded that sufficient information existed on health effects, and evidence of high potential for exposures to support recommendations for controls, and medical and environmental surveillance currently not in the OSHA regulation. While the document did not recommend a new exposure limit, it did recommend additions to the current standard.

The document emphasizes the need for more research on health effects from cobalt exposures and attempts to bring this to the attention of the research and occupational communities as a first recommendation. Likewise, to assure that adequate protection is provided to workers from exposure to cobalt, engineering controls and work practices are extensively discussed. Illustrations for process enclosure and/or exhaust ventilation are provided as guides in implementing engineering controls.

Question: Has NIOSH issued or does it have any plans to issue a recommended lower exposure limit for cobalt, and if not, why not?

Answer: Research needs, which were identified in the NIOSH cobalt document, will be considered in the NIOSH priority-setting process for future implementation of research activities. In addition, external research is being conducted on cobalt and its compounds will continue to be followed. As further studies on cobalt become available, NIOSH will periodically evaluate them. Should this information alter the perception of the seriousness of the hazard, and demonstrate that workers exposed to cobalt are not adequately protected by the present standard, NIOSH will re-examine the issues and consider proposing recommendations for a change in the standard.

Question: When did NIOSH begin work on assessing the hazards of cobalt?

Answer: Field investigations began in 1972.

Question: Has NIOSH conducted any research to determine the toxic effects of various cobalt compounds?

Answer: Prior to the initiation of the criteria document on cobalt in 1979, four Health Hazard Evaluations were conducted by NIOSH during the period of 1972 to 1978. In the course of these studies, occupational exposures to cobalt and cobalt compounds were characterized. In addition, in 1976-1977 NIOSH performed an industrial hygiene study of the nickel industry to identify and qualify exposure to airborne contaminants, including exposures to cobalt. In 1973, a final contract study report was received by NIOSH on a chronic animal inhalation toxicity study using cobalt metal powder at concentrations of 0.1 mg/cu m and 1.0 mg/cu m. The outcome of the chronic inhalation study along with the results of the environmental exposure characteristics served as the basis for NIOSH's development of the cobalt document.

Question: Does NIOSH currently have any plans to conduct laboratory research or epidemiologic studies on cobalt?

Answer: NIOSH has no plans to conduct in-house laboratory research or epidemiologic studies on cobalt. However, NIOSH will continue to monitor through its surveillence networks any new information developed on cobalt.

Question: Are you aware of any research now underway that will provide NIOSH with sufficient evidence to recommend lowering the current limit for cobalt exposure?

Answer: NIOSH is providing funds under contract for a study to evaluate exposures in the cement industry. This study, which is to be completed in 1982, is to identify airborne contaminants, including exposures to cobalt and identify the respective occupational groups of risk.

Question: What steps are NIOSH taking to assure that workers are being protected while cobalt research is underway?

Answer: To assure that adequate protection is provided to workers from exposure to cobalt, engineering controls and work practices are recommended to OSHA as modifications to the existing federal standard in the recent NIOSH criteria document. Illustrations for process enclosure and/or exhaust ventilation are provided as guides in implementing the recommended engineering controls.

NIOSH DOCUMENTS

Question: Please describe the difference between a criteria document, occupational hazard assessment, current intelligence bulletin, alert, special hazard review, and recent literature review.

Answer: A criteria document is the principal vehicle used for the formal transmittal of Institute recommendations to OSHA regarding workplace exposure to chemicals and other agents. In most cases each document addresses a single chemical, but in some cases a single document addresses several related chemicals. NIOSH has also produced criteria documents that have addressed situations other than chemical exposure; the document on work in confined spaces is an example of that kind of criteria document. Criteria documents are by necessity comprehensive in their description and evaluation of all available information on a subject. The criteria document also serve as a means of disseminating NIOSH recommendations more generally.

There are, however, instances when information becomes available to NIOSH that requires rapid dissemination to those responsible for occupational safety and health. In most cases, the available information is not extensive, but it does warrant publication to notify those concerned of a specific emerging issue. Current Intelligence Bulletins serve this purpose. They are designed to disseminate new information as rapidly as possible and as a consequence, they offer little evaluation data.

Occupational Hazard Assessments are somewhat similar to criteria documents. These documents do contain recommendations for specific procedures to control hazards in the workplace, but are not necessarily directed at a single substance.

The Health Hazard Alert was an experimental joint effort between NIOSH and OSHA to alert the occupational health community to potential workplace health hazards. These Alerts were directed to a wider audience than the NIOSH Current Intelligence Bulletins (CIB's). NIOSH provided OSHA with some technical assistance and printed as NIOSH publications, although technically they were OSHA documents. OSHA eventually developed their own independent system from this experiment.

Special Hazard Reviews (SHR) are done to provide in-depth treatment of special problem areas, such as carcinogenicity. The SHR had been developed to answer the criticism that criteria documents alone did not meet the information needs of a broad audience. These documents are prepared in a more usable information format for this audience and not in the regulatory format of a criteria document.

Recent Literature Reviews are exactly what their title implies, review of recent literature. They are designed only to present information and not make recommendations nor provide evaluations of the information.

It should be noted that since 1981 the NIOSH Division of Standards Development and Technology has been assessing this multiplicity of document types and is currently planning to produce only criteria documents, current intelligence bulletins and as appropriate, criteria document updates. This is being done in part to eliminate possible confusion over NIOSH's intent when these documents were produced. Despite the fact that many of these documents did not make recommendations for workplace environmental exposure limits for a specific chemical, they still contained other recommendations for such things as work practices, engineering controls, protective equipment and clothing, and training.

Question: Which of these documents actually recommends a safe exposure level to OSHA, as is required by the Occupational Safety and Health Act?

Answer: The criteria document is the primary instrument by which NIOSH fulfills its obligations as specified in Section 22 of the Occupational Safety and Health Act. It should be noted that the recommendations provided in a criteria document do not guarantee a safe exposure level per se. The final recommendation consists of many parts, of which the recommended exposure limit is only one. They also include recommendations for sampling and analysis, engineering controls, work practices, labeling, posting, informing employees, and when appropriate medical monitoring. NIOSH criteria documents present and evaluate the most current information available. Such information should not be expected to remain constant. What is believed to be "safe" by current standards may through further research be determined to be inadequate ("unsafe") in the future.

Question: When was the last time that NIOSH issued a document that recommended a safe exposure level?

Answer: The last document containing a "recommended" exposure level was "Criteria for Controlling Occupational Exposure to Cobalt," published early FY 1982.

Question: What was the frequency of issuing such documents during the last five years?

Answer:

	Document Type		
Calendar Year	Criteria Document	Current Intelligence Bulletins	Miscellaneous*
1977	24	2	0
1978	23	12	1
1979	1	3	0
1980	1	0	2
1981	4**	3	11
TOTAL	53	20	14

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* Includes: Alerts, Worker Bulletins, Criteria Document Literature Update, Special Reports, Information Bulletins, Guidelines, Special Occupational Hazard Reviews, Special Occupational Hazard Reviews with control recommendations.

** Includes two Occupational Hazard Assessments (Coal Liquefaction and Rendering) and two Special Reports (Field Sanitation and DEHP). Each contained recommendations to OSHA.

Question: What accounts for the decline in activity in recent years?

Answer: The decline in documents production in recent years is due to a number of factors. In 1976, 1977, and 1978, documents were developed according to a strict and demanding schedule. While a few of those documents were produced in-house, the majority were produced by contract. Since 1978 the number has been declining as a result of changing program emphasis and declining resources.

TRANSFER AUTHORITY

Question: Do you have an indication as to whether any States are taking advantage of the provision in the law allowing them to transfer funds from the Preventive Health and Health Services block grant to other health grant programs?

Answer: We have no information at this time that any State has utilized the provision in the law allowing for the transfer of funds from the Preventive Health and Health Services block grant to other health grant programs. Most States are continuing historical funding patterns during 1982, and developing procedures for determining future funding priorities and patterns.

BLOCK GRANT AND INDIAN TRIBES

Question: To what extent have Indian tribes taken advantage of the provision in the law to apply directly for funds under the Preventive Health and Health Services block grant?

Answer: To be eligible for direct funding under the Preventive Health and Health Services block grant, an Indian tribe or tribal organization had to receive a grant directly from the Secretary in FY 1981 under any of the programs replaced by the Preventive Health and Health Services block grant. The Santee Sioux Tribe of Nebraska and the Kickapoo Tribe of Kansas were the only tribes eligible for direct funding in FY 1982. Each tribe has submitted an application and has been approved for direct funding.

Question: Have any allocations to States under the Preventive Health and Health Services block grant been contested because of reductions made to accommodate direct grants to Indian tribes?

Answer: The States of Kansas and Nebraska have each been notified of the pending awards to be made to the two Indian tribes. They have not contested the direct funding of the grants to the tribes.

Question: Have direct grants to Indian tribes presented any other particular problems in the Preventive Health and Health Services block grant?

Answer: Initially, there was a misunderstanding among the various Indian communities concerning the eligibility requirements under the Preventive Health and Health Services block grant. CDC received 200 letters of intent to apply and numerous telephone calls from the Indian tribes and tribal organizations requesting information on the application for direct funding under the block grant authority - even though only two tribes are eligible.

Letters were sent to the eligible tribes identifying the application process and deadline. The ineligible tribes were notified of the basis for their being ineligible.

VENEREAL DISEASE

Question: Last year, you testified about the success of the Venereal Disease Program in the area of gonorrhea control. I understand that Oregon is one of the states where gonorrhea rates have been reduced in the last five years. Will the FY 1983 budget enable continued success in the control of gonorrhea?

Answer: In FY 1983, venereal disease control programs will continue to place emphasis on the control of gonorrhea and its severe complications. Gonorrhea screening and epidemiologic services will focus on young patients with their first infection; patients with repeat infections; and, women with gonococcal pelvic inflammatory disease. Support will continue in major metropolitan areas for programs to prevent and control gonococcal pelvic inflammatory disease including rapid identification of gonococcal PID patients seen as hospital outpatients; counselling patients to encourage adherence to treatment and posttreatment testing schedules; ensuring that all patients receive an appropriate medical followup to determine their clinical response; thoroughly interviewing patients to identify all "at-risk" sex partners; and, rapidly referring sex partners of patients for diagnosis and appropriate treatment. The surveilliance system for penicillinase-producing Neisseria gonorrhoeae (PPNG) will be strengthened by intensifying laboratory surveillance, screening efforts, case followup and referral services.

The trend in reported gonorrhea cases should not increase significantly. Approximately eight million persons will be culture tested. An estimated 300,000 persons with a positive test will be treated. Approximately 200,000 additional persons will be examined through followup contact tracing/partner referral activities with 170,000 of these receiving treatment. Screening, followup and outreach efforts will prevent over 200,000 new cases of gonorrhea.

Question: Has the success of the gonorrhea control program been at the expense of programs to deal with other sexually transmitted diseases?

Answer: Existing control programs try to focus on the greatest possible prevention of cases and serious complications.

In FY 82, major efforts have been directed toward women who have gonococcal pelvic inflammatory disease, the major cause of infertility due to a sexually transmitted agent. Both initial and followup health care for these women have been improved and have reduced the severity of initial complications. Their sexual partners are being referred, examined and treated in order to reduce the risk to women of recurrent bouts of this condition.

Some resources formerly devoted to syphilis control activities have been redirected to the control of penicillinase-producing Neisseria gonorrhoeae (PPNG) and the prevention of the outcomes of gonorrhea, such as infertility, and to renewed emphasis on VD services for prenatal patients.

There is also a need to address the prevention of another treatable STD, Chlamydia trachomatis infection. This, like gonorrhea, is a major cause of pelvic inflammatory disease. Besides providing training for medical care providers to improve diagnostic and case management skills and encouraging all VD clinics to provide diagnostic and treatment services, CDC is developing, in two selected sites, the first phases of pilot programs for the prevention of infections and complications of Chlamydia trachomatis. These pilot programs consist of: Screening asymptomatic women at high-risk for sexually transmitted diseases, those who have pelvic inflammatory disease, or those who are pregnant; and testing their male sexual partners for chlamydia; and providing diagnostic, therapeutic, counselling and case management services for infected patients and their sexual partners.

Herpes is a somewhat different problem. No adequate drug exists for the treatment of infected persons. Thus, applied research, patient education, and training of VD clinicians have been stressed. To make VD clinicians knowledgeable, diagnosticians as well as sensitive patient counselors is the objective of the recently developed, CDC-sponsored network of STD prevention/ training clinics.

Question: How serious is the problem of congenital syphilis today?

Answer: There had been a progressive fall in the rates of congenital syphilis among infants from 1971 through 1979. However, in FY 1981, the rates increased to 5.1 from 3.2 cases per 100,000 live births in FY 1980 (an all-time low).

Congenital syphilis among infants can be prevented by reducing the incidence of syphilis (especially among women) in the general community; proper prenatal care; prenatal serologic testing in the third trimester; and, timely and thorough epidemiologic followup of expectant mothers and of fathers who are contacts of infectious syphilis cases.

The increase in congenital syphilis is believed due to a shift in resources from syphilis to gonorrhea and failure of the prenatal care system - lack of serological testing during the prenatal period or a need for serologic testing, both in the first and last trimester of pregnancy.

Question: What happens to a newborn with congenital syphilis?

Answer: A significant portion of newborns with congenital syphilis will be stillbirths. Of those born alive, the earlier the onset of symptoms, the poorer the prognosis and the more likely they are left with permanent neurologic damage. Early signs and symptoms may include skin lesions, highly infectious mucous membrane lesions of the nose and mouth, inflammation of the long bones, anemia, enlargement of the spleen and liver and central nervous system involvement.

TREATMENT-RESISTANT VD

Question: A new problem which seems to be of great concern, particularly in large cities and on the West Coast, is penicillin-resistant gonorrhea. How serious is the problem?

Answer: Since its recognition in March of 1976, a total of 4,137 cases of penicillinase-producing Neisseria gonorrhoeae (PPNG) have been reported from 47 States, Guam and the District of Columbia. From January to October of 1981 alone, there were 2,165 cases reported; a 154.7 percent increase from the same period of 1980. This continuing trend is due to both increases in disease importation and sustained domestic transmission in a number of major metropolitan areas, although intensive efforts to control major outbreaks are showing promising results. Although PPNG infections constitute only 0.25 percent of all gonorrhea cases in the United States, disease importation and subsequent transmission within the United States can be expected to continue. The major threat posed by the advent of these new strains is the loss of penicillin or ampicillin as an inexpensive, highly effective, single session treatment for gonorrhea. Previously, only occasional strains of gonorrhea resisted moderately large doses of penicillin. These new strains are resistant to even massive doses of all forms of penicillin. Should PPNG strains become the dominant strains of gonorrhea in the United States, the incidence and costs of complications and the difficulty of gonorrhea control would be enormously increased. For example, it costs three to four times as much to treat a single case of gonorrhea with spectinomycin as it does with the cheapest penicillin treatment.

Question: What is CDC doing to try to develop successful treatments of penicillin-resistant gonorrhea?

Answer: In addition to monitoring the resistance of gonococcal strains to penicillin and other recommended therapeutic drugs, CDC supported research sites are continuing to participate in trials of alternate therapies, predominantly cephalosporins, for the treatment of penicillin-resistant gonorrhea.

HEALTH HAZARD EVALUATIONS

Question: One recommendation of the Public Health Service's 1990 Objectives for the Nation is that the number of Health Hazard Evaluations performed annually should increase to 1500. The FY 1983 budget, however, reflects a significant decrease from FY 1982 for all NIOSH activities. How many health hazard evaluations was NIOSH able to conduct?

Answer: Health Hazard Evaluations are a top priority of CDC and over the last few years, NIOSH has been progressively moving toward the goal of performing 1500 health hazard evaluations (HHE's) per year by 1990 in general industry and mining operations. In fiscal year 1981, NIOSH conducted 359 HHE's, compared with 200 investigations completed in FY 1979.

Question: How many requests did you get for such evaluations?

Answer: NIOSH received 513 requests for health hazard evaluations in FY 1981, compared with 230 in FY 1979.

Question: What effect will the budget decrease for FY 1983 have on the number of Health Hazard Evaluations you will be able to conduct?

Answer: In fiscal years 1982 and 1983, NIOSH plans to keep the level of resources allocated to the HHE program constant, reducing NIOSH resource allocations for other lower priority programs. To date, NIOSH has been able to cope with increasing numbers of HHE's mainly through increasing the productivity of our investigators. In fiscal year 1983, NIOSH plans to make concerted efforts to strengthen the capabilities of State Health Departments to conduct health hazard evaluations. In addition, we will continue to use cooperative agreements, medical service contracts, and medical officers in the EIS program to supplement in-house staff. These efforts should continue to result in further increases in the numbers of evaluations. We expect to be able to sustain a level of 500 HHE's per year over the next two years.

Question: Who is more likely to request such evaluations: workers, or employers?

Answer: In FY 1981, approximately 20 percent of NIOSH requests for HHE's were from employers, 50 percent from employees and/or unions; 25 percent from other government agencies; and 5 percent from other sources. Over 20 percent of these requests were from small businesses. The 20 percent of requests from employers represents a signficant increase over FY 1980, when only 12 percent of the requests were from employers. We expect that these proportions will remain essentially the same in the future.

BIRTH DEFECTS

Question: To what extent can the incidence of birth defects be attributed to occupational risk?

Answer: The social, economic, and personal burdens of sterility, spontaneous abortions and mental, physical and biochemical congenital defects are well recognized. The March of Dimes estimates that approximately 15 million Americans are affected by some form of birth defect, including mental retardation, structural malformations and errors in metabolism. Their estimates indicate that 200,000 infants (7% of all live births) are born annually in the United States with some kind of defect. As noted in the table below, it has been estimated that 30-35% of birth defects are attributable to known causes; 7-11% of these known causes are traced to an environmental component. The majority of defects, 65-70%, have no discernable cause.

Known Causes of Birth Defects

Environmental Causes	
Radiation	1%
Infections	2-3%
Maternal metabolic embalance	1-2%
Drugs and environmental chemicals	2-3%
Known Genetic Transmission	20%
Chromosomal aberration	3-5%
Potentiative interactions	?
Unknown	65-70%

Source: Wilson, James G. (1973). Environment and Birth Defects. Academic Press, New York.

From these data, it is not possible to estimate the incidence of birth defects attributable to occupational risk(s). However, it is known that more than 1,000 new chemical compounds are developed each year and are added to the approximately 30,000 chemicals and 2 million mixtures, formulations and blends already in commercial use; many of these could have teratogenic and reproductive failure potential. For example:

- NIOSH has identified in the workplace 146 chemicals that are cited as "teratogens" in the 1979 NIOSH Registry of Toxic Effects of Chemical Substances. It is estimated that 24,000,000 workers are potentially exposed to one or more of these chemicals.
- NIOSH studies have established that these potential exposures are common to both male and female workers.
- NIOSH studies have established that the cause of reproductive failure is common to both males and females.
- Eight percent of NIOSH health hazard evaluations in fiscal year 1981 were in response to suspected reproductive problems, such as clusters of spontaneous abortions.
- Epidemiologic studies have uncovered relationships between occupational hazards and reproductive effects (e.g., malformations in offspring of operating room personnel and spontaneous abortions in this group of workers; sterility of male workers exposed to dibromochloropropane; gynecomastia and reduced libido in males manufacturing oral contraceptives and DES).

Question: How has NIOSH contributed to improvements in the workplace which reduce the risk of birth defects?

Answer: Based on the concerns mentioned above, NIOSH has been investigating reproductive hazards since 1976-77 and formally adopted a Reproductive Effects Research Initiative in Fiscal Year 1981. Funds attributed to this program in Fiscal Year 1981 and 1982 are $1.5 million and $3.4 million, respectively. In Fiscal Year 1983, this activity is expected to remain at approximately the same budget level. The following is a brief summary of NIOSH's activities since 1976.

During 1976-78, NIOSH's main contribution in this field consisted of the publication of two documents: "Guidelines on Pregnancy and Work," which was prepared for NIOSH by the American College of Obstetricians and Gynecologists, and the "Proceedings of a Workshop on Methodology for Assessing Reproductive Hazards in the Workplace." These initial efforts brought this subject to the attention of the scientific community, industry, labor unions and the public in general, and further increased the awareness of the problem within NIOSH.

Under the current Initiative, we are involved in a research program that has four main objectives: (1) to define the biochemistry of mutagenesis and teratogenesis; (2) to screen large numbers of chemicals for mutagenesis, teratogenesis, transplacental carcinogenesis, fertility inhibition, ability to lower birth weight, and ability to alter sex ratio; (3) to identify workers who are potentially exposed to reproductive hazards and to aid in designing controls for those hazards; and (4) to identify groups of workers with abnormal reproductive experience and subsequently to determine the probable causes of those adverse outcomes.

This research Initiative combines the efforts of the NIOSH toxicology laboratories and epidemiology groups which conduct surveillance efforts and field studies of workers potentially at risk.

Since this research activity is relatively young, it is not possible to estimate the impact which NIOSH has had on reducing the risk of birth defects and reproductive hazards. However, NIOSH's program has contributed significantly to the Nation's effort (which includes other government agencies, universities, and private scientists) of identifying reproductive hazards, identifying occupational groups potentially at high risk due to reproductive effects, and, most importantly to date, developing new epidemiologic and laboratory techniques. The results of these efforts have been disseminated through conference presentations, publications in scientific journals, and recommendations to industries, labor and the Occupational Safety and Health Administration. Based on this increase in information, the foundation to begin lowering the risk of birth defects and decreasing reproductive hazards as a result of occupational exposure has been created.

JOB STRESS

Question: Do you believe the problem of job stress to be a legitimate Federal concern?

Answer: Yes, job stress should be a Federal concern because it is a major contributor to ill health in the U.S., and there is growing research evidence linking job demands and faulty work design to stress-related disorders in the nation's workforce. Examples for highlighting include:

(1) Coronary heart disease, recognized as a major stress-related problem, accounts for 38% of all deaths in the United States, 27 million lost workdays, and over $80 billion in estimated productivity losses and medical/insurance costs to the nation's economy each year. A number of occupational conditions and work activities are implicated as risk factors in the occurrence of coronary heart disease. These include undue workloads, paced work, time pressures, and related factors.

(2) Psychological impairment is increasing as witnessed by a rise in worker compensation claims for both acute and chronic psychiatric disability. Fifteen states now make disability payments to workers suffering from work-related mental disorders. Factors in the work environment associated with these problems include paced work regimens, non-utilization of skills, and repetitious or boring tasks.

(3) Spreading automation and new technology in the workplace are causing major changes in job tasks and organizational structure with new forms of stress emerging (e.g., closer monitoring of one's performance, task-imposed isolation, threat of job loss, high cognitive or sensory-motor demands). Worker dissatisfaction with their jobs, behavioral problems and symptomatic health complaints mark such stressors which could portend more serious health problems. Over 50% of the U.S. workforce is now engaged in white collar work, which is being effected by the new technological revolution brought about by computers, thus giving further impetus to the need to study job stress problems and means for their alleviation.

The problem of job stress is common to such a diversity of occupations and industries that only a Federally supported effort can provide needed viability. The workplace not only provides a unique opportunity to study a wide variety of stress problems in a diverse population, but also provides access to large numbers of people for health promotion and stress reduction programs. The Occupational Safety and Health Act provides that NIOSH conduct research into the causes of job stress and means for its amelioration. NIOSH has been carrying-out such activities for ten years and has a recognized, successful track record. NIOSH has taken the lead in the area of job stress research and control measures.

Question: What high risk occupations are under review by NIOSH for stress-related disorders?

Answer: Over the past ten years, NIOSH has evaluated a variety of allegedly high risk occupations such as air traffic controllers, nurses, quality control inspectors, letter sorters, sales workers and police officers to define stress producing job factors and their health outcomes. In the course of this research, it has become evident that there are certain job features common to many of these occupations that are significant contributors to worker distress. Lack of control over the work processes, paced work, shift work and worker isolation from peers are among the more salient stress-producing factors that have been isolated by NIOSH research. Given this experience, it is believed more prudent and cost effective to focus studies on these job factors and their health implications as they may occur across work situations, rather than highlighting a particular occupation for examination. Therefore, current NIOSH stress research activity concentrates on work factors rather than on particular occupations. In this regard, aspects of worker stress and strain are being addressed with respect to the following job factors:

(1) Machine-paced work
(2) Office automation and computerization of office work
(3) Information processing jobs that are affected by automation
(4) Video display terminal work
(5) Alternative work schedules

These research activities may key on particular occupations that have uniquely stressful working conditions that will require separate analysis. However, the general strategy is to examine work processes rather than individual jobs so that information can be generalized across various jobs for maximum benefit at minimum cost. In addition to this problem defining work, efforts are also ongoing to develop techniques for reducing job stress through coping strategies as well as job redesign.

EPIDEMIC CONTROL

Question: Will the FY 1983 budget request for epidemic services reflect a decrease in the level of epidemic control compared with the level of activity in previous years?

Answer: No, we anticipate that the 1983 budget request will allow us to support epidemic services at the same level as in 1982. We will be able to meet the objectives we have for these programs and to respond fully to State and local health authorities' requests for epidemiologic and investigative laboratory assistance.

Question: Will the number of Epidemic Intelligence Service officers be sufficient to carry out their mission of investigating all potentially serious outbreaks?

Answer: While it is not possible to accurately predict the frequency or scope of health emergencies, we are confident that the number of officers assigned to the Epidemic Intelligence Service during 1983 will be sufficient to meet the most pressing requests for the investigation of disease outbreaks and other preventable disease conditions. We currently have 114 officers assigned to the

Epidemic Intelligence Service. During 1983, we will have 108 EIS officers. However, this slight decrease is within the limits of normal fluctuations we have experienced in recent years and will not seriously limit our ability to respond to requests for epidemic assistance.

Question: How have our priorities in epidemic control changed in the last few years?

Answer: Conceptually, our priorities have not changed regarding epidemic control since our mission is to respond to requests and needs for epidemic assistance as they occur regardless of cause. Epidemic control activities are required to control possible epidemics, and are not dictated by priorities, per se, but guided by the nature of requests made by State and local health authorities. As would be expected with the success of the immunization program, during the last few years, State health departments have experienced a decrease in outbreaks related to the immunizable diseases. At the same time, there has been an increase in State activities related to disease conditions associated with the environment and the workplace. This shift is reflected in CDC's activities as we have had a continual increase in the number of investigations related to the environment and the workplace, and thus, a proportional decrease in the number of infectious disease outbreaks investigated. Each request for assistance in investigating a disease outbreak or a special health problem continues to receive high priority. The extent of our involvement is by and large dictated by the size of the problem and the complexities of the disease under investigation.

Class IV viruses, i.e., Lassa Fever and Ebola viruses, continue to be a special problem if they are imported from Africa. We are continuing to study these viruses to develop prevention, treatment, and control method to recommend if they spread to this country.

ALCOHOL AND DRUG ABUSE

Question: One of your targets in the area of Epidemic Control is the high incidence of alcohol and drug abuse. What control activities will the FY 83 budget support in the area of alcohol and drug abuse?

Answer: "Misuse of Alcohol and Drugs" is one of the five health promotion target areas identified in the Surgeon General's National Prevention Objectives for 1990. Because alcohol is a prominent risk factor for a wide variety of the health problems that need to be dealt with in the 1980s, CDC will combine its strength in applied epidemiology and its cooperative relationships with State health agencies is engaged in limited epidemiologic research related to alcoholism. CDC coordinates its activities with the National Institute of Alcohol Abuse and Alcoholism, other Federal agencies, and academic centers to generate basic epidemiologic knowledge about alcoholism which might in time lead to improved methods of prevention and control. Working to address the problem of alcohol abuse and alcoholism, CDC will:

1) review and evaluate epidemiologic studies in alcoholism and its effects; and

2) design and evaluate methods of surveillance for alcoholism and its effects;

These activities will be coordinated with other current CDC activities in which alcohol is a factor:

1) evaluation of genetic factors in alcoholism;

2) impact of alcohol use and alcoholism on performance and health in the workplace;

3) impact of alcohol use and alcoholism on accident and injuries;

4) impact of alcohol use and alcoholism on selected infectious disease problems such as tuberculosis; and

5) impact of risk-reduction programs on alcohol-associated morbidity and mortality.

This small investment in epidemiology will be closely linked to prevention techniques developed and disseminated at CDC under other budget activities--e.g., technical assistance and consultation provided to States carrying out health education and risk reduction programs under the Preventive Health and Health Services Block Grant.

Many States plan to continue demonstration projects to deter smoking and misuse of alcohol among children. Alcohol as a risk factor is also addressed in school health education and Health Risk Appraisal, both important prevention methods, and is one of the risk factors covered by the States and CDC in risk factor prevalence surveillance.

STRESS AND VIOLENT BEHAVIOR

Question: One of the stated objectives in the 1979 report of the Surgeon General, Healthy People, is to reduce the incidence of stress and violent activity in our country. Your FY 1983 budget document indicates that this area remains a high priority. How do you plan to address the health problems of stress and violent activity in the '83 budget for the Centers for Disease Control?

Answer: The publication, Healthy People, cited several target problems to be addressed regarding stress and violence in the United States. These included homicide, suicide, and child abuse.

CDC has begun to examine these problems epidemiologically, and will do the following:

1) Determine persons at greatest risk of these forms of violence, using national data sets;

2) Determine the correlates of these risks, especially those that may be amenable to intervention/prevention measures;

3) Design cost-effective pilot intervention/prevention projects based on these findings; and,

4) Evaluate the effectiveness of these projects using the parameters of morbidity and mortality due to violence as measurable endpoints.

Question: Do you plan to enlist other Federal agencies such as the Department of Justice and the National Institute of Mental Health in the effort?

Answer: CDC already is collaborating with a number of other Federal agencies in this effort. The most long-term interactions have been with the National Center for Health Statistics (NCHS), which provides CDC with national vital statistics mortality data tapes on homicide and suicide, and with the Federal Bureau of Investigation's Uniform Crime Reporting Program (FBI-UCR), which provides CDC with national law enforcement homicide data. CDC also has on-going interaction with the National Center for Child Abuse and Neglect (NCCAN, HHS), concerning our activities in the area of child abuse. We recently have had several meetings with the Department of Justice and the National Center for Mental Health (NIMH), to initiate collaboration and coordination of our efforts in this area. CHPE and CDC have also met with the Family Advocacy Committee at the Department of Defense to offer our assistance in implementing a military child abuse registry. The spirit of cooperation has been strong at these meetings, and all these agencies agree that collaboration will prevent duplication of effort and will help all agencies coordinate the direction of our activities.

EPIDEMICS

Question: There have been alarming reports recently about the outbreak of a new, often fatal, illness which attacks and suppresses the immune system of seemingly healthy people, making them highly susceptible to damaging infections that otherwise would only be mild. According to a February 25 Wall Street Journal article, of 251 reported cases, 99 victims have died. How dangerous is this disease to the public health?

Answer: Although the full extent of this disease is not yet known, it is highly dangerous for persons getting the disease. At the present time, the disease is concentrated among homosexual men; however, 10 percent of the cases have been reported among heterosexual men and women. Forty percent of the victims of this disease have died. During the last 3 months, the CDC has received reports of an average of one case per day and one fatality every 2 to 3 days.

Question: What do we know about this disease?

Answer: In June 1981, the CDC became aware of the occurrence of several highly unusual illnesses among previously healthy persons in the United States. One illness has been a type of cancer called Kaposi's sarcoma (KS). The other illnesses have been life-threatening infections, the most frequent of which has been Pneumocystis carinii pneumonia (PCP). About 10 percent of affected persons have had both KS and PCP. These persons have been shown to have serious impairments of their immune systems; the underlying cause of this immunosuppression is unknown.

The earliest cases of KS and PCP were diagnosed in 1979. Of the 268 cases now reported to the CDC, 82 percent were diagnosed since January 1981. Although cases have been reported from 17 States, over three-quarters of the cases have been residents of New York City, Los Angeles, and San Francisco. The average age of cases has been 35 years. Approximately 80 percent of the cases have been homosexual men.

The CDC is carrying out epidemiologic and laboratory studies to attempt to determine the risk factors for these serious illnesses.

Question: Are victims of this illness more likely to develop cancer?

Answer: Approximately half of the cases reported to CDC have developed Kaposi's sarcoma, a type of cancer which has been previously associated with impairments of the immune system in other groups of patients. Since Kaposi's sarcoma has been associated with other cancers, particularly lymphomas, we are currently investigating recent reports of other unusual cancers occurring in the same populations.

BUILDINGS AND FACILITIES

Question: What system do you use for determining priorities in making improvements on CDC buildings and facilities.

Answer: The CDC Facility Planning Board monitors the facilities to determine the repair and improvement requirements, including safety, handicap, and energy saving projects. Each project is analyzed and ranked in priority order to assure the accomplishment of those projects which are mandatory to protect the health of CDC employees, the environment, and the facility investment of the Government.

Question: What priority improvements will be made in CDC's facilities in FY 1983?

Answer:

Clifton Road, Atlanta, Georgia:

1. Remove the asbestos hazard in Bldgs. 2 & 6.	100,000

2.	Incinerator modifications and repair, and stack replacement - Building 6. The incinerator is presently inoperative because of major stack damage. Repair and modification to comply with current requirements is essential.	150,000
3.	PCB removal from ten (10) transformers.	175,000
4.	Clean room assembly and space modification for lyophilizer operation.	30,000
5.	Walk-in freezer replacement, Building 1. The existing freezer is more than 20 years old.	25,000
6.	Chilled water interconnect - office system to main chilled water plant which will allow the office to be air conditioned from the main chilled water plant should the office chiller (now 22 yrs. old) fail.	45,000
7.	Reset coping, repair/replace caulking, exterior of all buildings.	50,000
8.	Resurface parking lots.	116,000

Taft, Cincinnati, Ohio:

1.	Modify ventilation system to provide one pass air system for laboratorian protection.	75,000
2.	Replace existing incincerator which fails to meet certification requirements.	50,000
3.	Provide standby chiller for the inhalation laboratory.	30,000
4.	Install additional boiler (Present boiler 30 years old).	53,000

Morgantown, West Virginia:

1.	Provide new ventilation system for respiratory laboratory to support program initiative in respirator research.	80,000
2.	Caulk exterior panels and windows.	25,000
3.	Replace existing distilled water system, which is now contaminated and is not being used.	22,000

Chamblee, Georgia:

1.	Ventilation system improvement, Bldg. 18. This work is required in order to provide a safe working environment for investigations involving dioxins.	50,000
2.	Fire detection/security improvements.	75,000
3.	Reroof several buildings.	64,000
4.	Cable system for word processors.	55,000

Lawrenceville, Georgia:

1.	Roof replacement, Bldgs. B, D, E.	60,000

San Juan, Puerto Rico:

1.	Emergency generator.	110,000

Miscellaneous:

Repair building equipment as required.	80,000

INTERNATIONAL HEALTH

Question: Under what authority does CDC conduct its international health activities?

Answer: CDC conducts its international health activities under the following authorities:

Direct Authorities

Sections 301, 307, and related sections of the PHS Act (42 U.S. Code 241, 242b).

Section 361 of the PHS Act (42 U.S. Code 264)

Delegable Authorities

Sec. 5, International Health Research Act of 1960 (22 U.S. Code 2103).

Sec. 104, Foreign Assistance Act of 1961 (22 U.S. Code 2151b).

Sec. 104, Agricultural Trade Development and Assistance Act of 1954 ("P.L. 480") 7 U.S. Code 1704).

Sec. 102, Mutual Educational and Cultural Exchange Act of 1961 (22 U.S. Code 2452b).

Question: How much do you plan to spend on international health in Fiscal Year 1983?

Answer: CDC has no budgetary line item for international health. Except for activities undertaken on a reimbursable basis with USAID or WHO (about $4.4 million in FY 1982), such as the former Smallpox Measles Program in West Africa, most of CDC's "international health activities" are inseparable from domestic functions. They are also carried out by the same people responsible for related, but purely domestic activities. Our leprosy specialist, for example, is concerned with domestic and international aspects of leprosy, as well as with Legionnaire's disease. Exceptions to that context are field assignments related to the study of Lassa fever in Sierra Leone (1 CDC staff) and study of malaria in Guatemala (2 CDC staff).

Question: Specifically, how does the U.S. public health benefit from your international studies, research, and assistance?

Answer: In general, CDC's international work benefits the U.S. by:

- Giving the U.S. an "early warning" system against special diseases, newly-resistant bacteria, or epidemics (e.g., "Russian Flu").
- Providing access to unique field situations (e.g., Lassa fever in Sierra Leone)
- Some experience obtained is applicable in U.S. (e.g., smallpox, measles control techniques)
- Manifesting U.S.'s humanitarian concern (e.g., Thailand refugee relief)

More specific examples of some U.S. benefits in 1981:

- Preparedness, defense against dengue fever in 1980, 1981 was facilitated by direct and indirect (PAHO) collaboration with Mexico, Cuba.
- Health education materials on dengue fever (in Spanish) from Mexico were adapted and used for controlling dengue in Puerto Rico.
- Joint CDC/NIH investigation of Toxic Syndrome in Spain may advance knowledge of pathogenesis of autoimmune infections.
- Identifying chloroquin-resistant malaria among American travelers returned from East Africa facilitated by research done in Kenya, Central America, Atlanta.
- Capacity for evaluating receptivity of host mosquitoes to dengue, malaria in California and Florida at sites of entry of large numbers of Indochinese and Haitian refugees made possible by international research experience.
- Methods for diagnosing, treating, and preventing spread of Lassa fever in the U.S. were developed by study of that disease in an endemic area of Siera Leone.
- In 1981, three suspected cases of hemorrhagic fever in U.S. (Washington, New York, St. Louis) were evaluated via specimens sent to CDC: Lassa ruled out. Also received specimens via couriers from three suspect cases in Canada (two in Montreal, other in Vancouver).

- Collaboration with Burma on testing hepatitis B vaccine only possible via WHO, WHO consultants, and WHO Collaborating Center at CDC/Phoenix.
- WHO Collaborating Center for Influenza, by receiving strains of flu isolated all over the world, is able to advise on and provide appropriate strains for flu vaccines for use by U.S. population.

Question: Could CDC achieve equivalent benefits by studying the same problems domestically?

Answer: No, the same benefits could not be achieved domestically, because in many cases the disease (Examples are Class IV viruses such as Lassa and Ebola virus) is not occurring in this country. To protect the American people when it does occur, the disease has to be studied so that prevention and/or treatment and control methods can be implemented when the disease does reach our country.

Question: How does CDC's international health activities differ from those of the Agency for International Development and World Health Organization?

Answer: The CDC's directly-funded international health activities are largely research projects oriented toward protecting the health of the American people. AID is most concerned with development projects, including large-scale health assistance. The World Health Organization serves as a facilitator, and provides a forum for consensus building internationally. It does not itself undertake research or conduct operational programs. We work closely, however, with both USAID and WHO.

AGENT ORANGE

Question: The Committee was pleased to learn of the Centers' efforts to study the possible impact of exposure to "Agent Orange" upon our nation's veterans. It is the Committee's understanding that previous efforts to study "Agent Orange" have not focused upon the possible different effects upon the two sexes. To what extent will CDC look specifically at the impact on female veterans of "Agent Orange"?

Answer: CDC has no studies that are specifically looking at female veterans. It is our understanding, however, from our work on the Agent Orange Working Group that women serving were for the most part medical personnel. The numbers of other women were relatively small. Women, medical personnel, and others generally served in areas where there was little chance of exposure to Agent Orange. The protocol being developed by the Veterans Administration for epidemiological studies required by Public Law 96-151 is now addressing this issue. If enough women are available, it would be reasonable to include them. If not, it would be more reasonable to exclude their participation.

NIOSH FUNDS

Question: Both the House and Senate bills for Fiscal Year 1982 prohibit the use of funds for a NIOSH move to Atlanta or Cincinnati. The intent of this language was very clear, yet I understand that, contrary to the law, several transfers and reassignments have taken place since October 1981. What movement of positions from Rockville to Atlanta has taken place? How many positions, and what positions?

Answer: Before October 1, 1981, eight permanent employees joined the NIOSH staff in Atlanta. Since December 15, 1981, when the Continuing Resolution containing language prohibiting the expenditure of funds for the transfer of NIOSH headquarters became law, no permanent employees have been added to the NIOSH staff in Atlanta. From October 1 through December 14, 1981, only essential staff support (9 permanent employees) was provided to key NIOSH officials who had transferred prior to October 1st to ensure continuity to the Institute's program. Still, none of these actions involved movement from Rockville to Atlanta. The following list provides detailed information about the NIOSH Atlanta staff.

CENTERS FOR DISEASE CONTROL
National Institute for Occupational Safety and Health
Atlanta Staff

PRIOR TO OCTOBER 1, 1981

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Office of the Director				
Millar, J.D., M.D.	Director	Permanent	07/13/81	Directs and administers the policies and program of the National Institute for Occupational Safety and Health.
Coker, B.	Secretary	Permanent (Detail)	08/23/81	Provides secretarial and administrative support to the Director, NIOSH.
Harris, E., Ph.D.	Deputy Director	Permanent	09/06/81	Assists the Director, NIOSH, in the accomplishment of program objectives and policies for the Institute.
King, J.	Secretary	Temporary Permanent	07/22/81 10/04/81	Provides secretarial and administrative support to the Deputy Director.
Shamblee, T.	Executive Officer	Permanent	09/06/81	Assists the Director, NIOSH, in the accomplishment of program objectives through resource management and administrative service.
Morrison, B.	Secretary	Temporary Permanent	08/20/81 10/04/81	Provides secretarial and administrative support to the Executive Officer.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Office of Administrative and Management Services				
Dunkin, D.	Supervisory Program Analyst	Permanent	08/23/81	Provides program and management analysis and staff assistance to the Executive Officer, NIOSH, in areas such as budget, project planning, policy development, and personnel.
Office of Program Planning & Evaluation				
Myers, M.	Director, OPPE	Permanent	09/26/81	Directs the staff responsible for the planning of the Institute's research program and for the monitoring, control, and evaluation of that program.
Dobbin, D.	Program Analyst	Permanent	09/26/81	Provides staff support and management assistance to the Director, OPPE, in the planning and evaluation of the Institute's research program in the control of occupational hazards.
Neuhaus, E.	Clerk Typist	Temporary	09/14/81	Provides clerical assistance on word processing equipment to OPPE.
Touch, R.	Senior Program Analyst	Permanent	09/01/81	Provides staff support and management assistance to the Director, OPPE, in the planning and evaluation of the Institute's research program in identification and surveillance of occupational hazards.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
		OCTOBER 1, 1981 TO PRESENT		
Office of Administrative and Management Services				
Adams, J.	Travel Clerk	Temporary	12/28/81	Provides administrative assistance in the area of travel to the Office of the Director, NIOSH.
Beaullieu, B.	Admin. Clerk	Permanent	12/13/81	Provides administrative assistance in the areas of budget and procurement to the Office of the Director, NIOSH.
Crochet, A.	Writer/Editor	Temporary (on loan)	11/23/81	Provides editorial assistance to OAMS and the Office of the Director, NIOSH.
Foster, B.	Admin. Clerk	Permanent	11/29/81	Provides administrative assistance in the area of personnel to the Office of the Director, NIOSH.
Sumner, A.	Acting Branch Chief, Mgmt. Systems Branch	Permanent (on loan)	01/04/82	Directs the staff responsible for the Institute's management information system.
Office of Program Planning & Evaluation				
Aral, S., Ph.D.	Biostatistician	Temporary	01/24/82	Assists in planning and evaluation of the Institute's research program in identification and surveillance of occupational safety and health problems.

NAME	TITLE	TEMPORARY/ PERMANENT	EFFECTIVE DATE	DUTIES
Darby, G.	Coding Clerk	Temporary (on loan)	11/30/81	Provides computer and clerical assistance to OPPE, NIOSH.
Groza, T.	Program Analyst	Permanent	12/13/81	Assists in the evaluation of major Institute programs and of resource administration.
Holstun, D.	Public Health Advisor	Permanent	12/13/81	Assists in the management of the Institute's program in the areas of identification and surveillance of occupational health hazards.
Medwin, H.	Clerk Typist	Temporary	10/01/81	Provides clerical support to the Director, OPPE, NIOSH.
Tozzer, N.	Writer/Editor	Temporary (on loan)	01/28/82	Provides editorial assistance to OPPE in the area of information dissemination and technology transfer.
Turenne, R.	Program Analyst	Permanent (TDY from Morgantown)	12/13/81	Provides staff support in the planning and evaluation of the Institute's program in the area of information dissemination and technology transfer.
Withers, P.	Program Analyst	Permanent	12/13/81	Assists in the planning and management of the Institute's program in the control of occupational hazards.

Question: Where did the agency obtain funds for the transfers which have taken place?

Answer: The Congressional prohibition applied to the transfer of staff from Rockville. After October 1, 1981, providing essential staff to support key NIOSH officials located in Atlanta prior to that date has not required the transfer of any employees from Rockville to Atlanta.

Question: I understand that contracts are now being administered from Atlanta, and that the duties of project officers have been reassigned from Rockville to Cincinnati personnel, although the contractors themselves are located in the Washington, D.C., area. Explain this arrangement.

Answer: A few permanent employees remain in the Contracts Section of the Office of Administrative and Management Services in Rockville. During this period of uncertainity, the CDC has had to take action to ensure the continuity of this important function. Until the issue of the transfer is resolved, CDC headquarters is assisting NIOSH by administering eleven active contracts. Three of these have been initiated in Atlanta; none of these contractors are located in the Washington area. Of the contracts that were transferred from Rockville, only three contractors are in the Washington area. Other contractors are located in Salt Lake City, Philadelphia, Fort Worth, and Augusta, Georgia. Geographic location has not interferred with the administration of these contracts.

Again, because of the uncertainity surrounding the transfer, in order to maintain program continuity, new long-term document development which would be most jeopardized by staff losses is being managed in Cincinnati. Only two contracts and two project officers were affected by this decision. However, the Institute's short-term document development program (i.e. current intelligence bulletins) is still managed in Rockville and the two project officers have been assigned duties in this area.

Question: I understand that several Rockville employees are required to work in Atlanta a few days each week. Since Congress prohibited the use of funds for a transfer, under what authority are you spending the money?

Answer: During this interim period, a certain amount of travel between Rockville and Atlanta has been necessary to preserve the continuity of the Institute's mission. Just as a few staff members have travelled from Atlanta to Rockville, a few have travelled from Rockville to Atlanta. This travel is program-related and has been necessitated by the delay in the transfer of function. No employee has been forced to travel to Atlanta. No employees from Rockville work in Atlanta on a regularly scheduled basis.

Question: I understand that the number of grants and contracts awarded by NIOSH has been cut in half. As I understand it, in the first half of the fiscal year, the number of grant awards is eight, and the number of contracts is thirty-nine. Corresponding numbers for Fiscal Year 1981 are eighty-eight and one hundred seventy-five, respectively, why have these been so dramatically curtailed?

Answer: The number of grants awarded in FY 1981 was eighty-six, of which sixty-one were research and twenty-five training. The number of contracts awarded in FY 1981 was ninety-eight. Fourteen of these 98 contracts were reimburable, so that only eighty-four were actually funded by NIOSH. To compare grants and contracts over an entire fiscal year with those awarded in the first half of any given year is misleading, since all training grants, most research grants, and most contracts are awarded later in the fiscal year. This is because it usually takes six months after a project is approved for a contract proposal to be advertised, for it to be negotiated, and for contracts to be awarded.

Ten grants have been awarded to date in FY 1982. When all of 1982 can be compared with all of 1981, we anticipate that the number of grants awarded will be approximately the same. The reduction in funds will have the greatest effect, however, on extramural research contracts. With funding cuts the number of contracts can only be reduced proportionately. Five new contracts have been awarded so far in FY 1982 and thirty-seven have been modified, for a total of forty-two.

NIOSH/OSHA/MSHA

Question: Briefly, what is the relationship between NIOSH and the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA) which are both in the Labor Department?

Answer: The Occupational Safety and Health Act and the Federal Mine Safety Health Act establish the basic relationship of NIOSH to these organizations. In general, NIOSH serves in a scientific/technical advisory role on matters relating to health and safety. NIOSH identifies safety and health problems, assesses hazards, conducts research, makes recommendations and promotes safe and healthful work practices. In carrying out these functions, NIOSH continues to maintain communications at the policy level with both OSHA and MSHA. Specifically at the working level, NIOSH staff are meeting with their OSHA counterparts in both the Safety and Health Standards Directorate. Additionally, NIOSH is working cooperatively with the Technical Services Directorate on several issues, including the effectiveness of respirators required in the various OSHA standards. With MSHA, NIOSH staff interacts on a quarterly basis with their Health Policy Planning Group and have representatives on seven Bureau of Mines/MSHA committees.

SUBCOMMITTEE RECESS

Chairman HATFIELD. The subcommittee will stand in recess until 2 o'clock when we will continue hearings on the fiscal year 1983 budget on health and human services.

Dr. FOEGE. Thank you, Mr. Chairman.

[Whereupon at 10:40 a.m., Tuesday, March 2, the subcommittee was recessed, to reconvene at 2 p.m., this same day.]

(AFTERNOON SESSION, 2:04 P.M., TUESDAY, MARCH 2, 1982)

HEALTH SERVICES ADMINISTRATION

STATEMENT OF JOHN H. KELSO, ACTING ADMINISTRATOR

ACCOMPANIED BY:
W. HARELL LITTLE, DEPUTY ASSOCIATE ADMINISTRATOR FOR MANAGEMENT
DR. EDWARD D. MARTIN, DIRECTOR, BCHS
DR. DANIEL F. WHITESIDE, DIRECTOR, BHPDS
RICHARD R. ASHBAUGH, ACTING DIRECTOR, BMS
ANTHONY L. ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DHHS
JOHN BODE, DEPUTY ASSISTANT SECRETARY FOR FOOD AND CONSUMER SERVICES, DEPARTMENT OF AGRICULTURE

SUBCOMMITTEE PROCEDURE

Senator RUDMAN [presiding]. The subcommittee will come to order. We will now hear testimony from John Kelso, Acting Administrator of the Health Services Administration. Mr. Kelso, it seems to me that a year ago I chaired this and you were Acting Administrator then. They have not filled this position?

Mr. KELSO. That is correct.

PREPARED STATEMENT

Senator RUDMAN. If you would go ahead with a summary of your statement. We will put your prepared statement in the record at this point.

Mr. KELSO. Yes.

[The statement follows:]

STATEMENT OF JOHN H. KELSO

I appreciate this opportunity to appear before you today to discuss our fiscal year 1983 budget request for the Health Services Administration. As you are aware, Mr. Chairman, this budget excludes the Bureau of Indian Health Service, which is heard by the Department of the Interior and Related Agencies Subcommittee.

The fiscal year 1983 budget request for Health Services is $1.6 billion, a decrease of $481 million below the comparable 1982 level.

In FY 1981, as a result of the Omnibus Budget Reconciliation Act, two Block Grants were authorized within the Health Services Administration - the Primary Care Block Grant and the Maternal and Child Health Block Grant.

Under the MCH Block Grant, nine categorical programs were consolidated. States now have the authority, the flexibility, and the responsibility to target resources to areas of greatest need within their States.

We are pleased that 53 States and jurisdictions have already taken over the administration of the Maternal and Child Health Block Grant, and that all States will be administering this block grant by the end of fiscal 1982. They have submitted their reports of intended expenditures, are securing whatever professional and technical assistance they need and in general, have their programs well underway.

The other Block Grant which was authorized, the Primary Care Block Grant, will become operational in 1983. With a view toward facilitating implementation of the Primary Care Block Grant, we have undertaken an intensive review of primary care projects to eliminate support for those which do not meet the standards of performance and which do not serve highest priority need areas. As a result of this review, we have already discontinued or phased out support for 125 projects. This will help assure that States take over only the most effective and needed projects and ensure maximum utilization of scarce resources. In addition, we have been in touch with the State Governments and State Medical Societies to secure their participation in this year's project review process. Finally, we have developed agreements with several States for their very intensive involvement in all aspects of project administration, monitoring and direction.

Enhancement of State authority and responsibility with respect to Family Planning has been underway for several years. In 27 States and the District of Columbia there is now a single agency responsible for Title X services, and in 23 of these the grantee is the State Health Department. At this time we are actively working with several other States and we expect a number of additional State-wide arrangements this year.

Our 1983 budget request is developed around proposed legislative changes that would expand both the Primary Care Block Grant and the Maternal and Child Health Block Grant. This expansion is needed in order that we might continue to reduce Federal administrative duplication and give States and local governments greater control over the use of Federal resources. Specifically, Mr. Chairman, our 1983 budget request is proposing that the three remaining categorical programs in the Bureau of Community Health Services - Black Lung

Clinics, Migrant Health Centers, and Family Planning - be transferred into the existing Primary Care Block Grant which currently consists of the Community Health Centers activity. We are asking for a total of $416.8 million for this newly proposed Primary Care Block Grant program.

We are also proposing that the Maternal and Child Health Block Grant be expanded to include the Women, Infants and Children and the Commodity Supplemental Food programs now administered by the Department of Agriculture. This revised block grant will be called Services to Women, Infants and Children. By combining WIC with the existing MCH block grant, the States will have the ability to target both health care programs and nutrition services to the most needy mothers and their children. We are requesting an appropriation of $1 billion for this program in 1983.

The 1983 budget request of $103.4 million for the National Health Service Corps will maintain the current field strength of 2,115 Federal salaried assignees. Approximately 1,145 scholarship obligors will be available for service in 1983, of which 330 are included in the private practice option. We have been very successful in our efforts to place individuals in private practice settings. In 1981, a total of 412 NHSC scholarship recipients took the private practice option which substantially exceeded our goals. By the end of FY 1983, we expect that over 800 health providers will be exercising their option to serve in a private practice setting. Since these individuals receive no direct Federal salary support, the PPO furthers the goals of the NHSC at minimal expense to the Federal Government.

Our budget request for 1983 includes $11 million for the National Health Service Corps Scholarship program. This budget level will support the tuition costs of all 953 continuing scholars. No new awards will be made in 1983. We believe that the scholarship recipients who are now in the pipeline and who will become available for service over the next four or five years will provide sufficient health personnel to meet the essential staffing requirements of the NHSC.

The remaining $56.5 million requested in this budget will provide for funding for several direct medical services programs: the National Hansen's Disease Center, Federal Employee Occupational Health, and the Payment to Hawaii for treatment of Hansen's Disease. Also included is funding for centralized management within the Office of the Administrator, and program support for the Bureau of Community Health Services and the Bureau of Health Personnel Development and Service.

Finally, Mr. Chairman, as a result of the proposed law program changes included in this budget, it will be possible for the Agency to reduce personnel and associated costs significantly. For example, 443 positions and $16.1 million are being eliminated from the program support activity of the Bureau of Community Health Services. Of that total, 304 positions and $11.3 million are associated with proposed law changes. The total employment within the Health Services Administration exclusive of the Indian Health Service will be reduced by 630 positions, from a level of 3,944 in 1982 to 3,314 in 1983. I should note that a reduction in the total number of positions cannot be directly translated into the number of people actually effected by the loss of a job. The Department will continue to assist people in finding alternate employment. Funds necessary for the program support and program management separation costs are included in a separate request within the appropriation of the Office of the Assistant Secretary for Health. These funds will be made available as necessary to support the appropriate separation costs.

Mr. Chairman, this concludes my opening remarks. At this time, my staff and I will be pleased to answer questions which you and the Committee might have.

BIOGRAPHICAL SKETCH

Home Address: 2332 North Early Street
Alexandria, Virginia 22302
(703) 379-6230

Business Address: Acting Administrator
Health Services Administration
Parklawn Building, Room 14-15
5600 Fishers Lane
Rockville, Maryland 20857

Birthdate: June 16, 1925 - Iowa City, Iowa

Education: State University of Iowa - B.A. 1949 and M.A. 1950

Experience:

1981 to present	Acting Administrator Health Services Administration, PHS, DHHS
1976 to present	Deputy Administrator Health Services Administration, PHS, DHHS
1973 - 1976	Director, Office of Regional Operations, Office of the Assistant Secretary for Health, DHEW
1971 - 1973	Associate Administrator for Management, Health Services and Mental Health Administration, DHEW
1968 - 1971	Assistant Administrator for Management, Health Services and Mental Health Administration, DHEW
1966 - 1968	Executive Officer, Public Health Service, DHEW
1962 - 1966	Assistant Executive Officer, BSS/Environmental Health, PHS, DHEW
1960 - 1962	Chief, Management Advisory Branch, BSS/EH, PHS, DHEW
1957 - 1960	Management Analyst, PHS, DHEW
1955 - 1957	Management Analyst, Department of Agriculture
1951 - 1955	Occupational Research Analyst, Department of the Navy

Awards

1969	DHEW, Superior Service Award
1972	DHEW, Distinguished Service Award

SUMMARY OF STATEMENT

Mr. KELSO. The budget before you, Mr. Chairman, for 1983 requests $1.6 billion. Significant changes in the budget include the expansion of the primary health care block grant to include the family planning, the black lung, and the migrant health programs; and the expansion of the maternal and child health block grant to include the women, infants, and children and the commodity supplemental food programs currently in the Department of Agriculture.

In addition, we are continuing the National Health Service Corps in 1983 at the 1982 operating level, with emphasis on the private practice option.

Also, we will be abolishing the Bureau of Medical Services in 1983 as a result of closing the PHS hospitals and clinics in fiscal year 1982.

Finally, we are requesting a reduction of 630 positions to reflect the block-grant changes and other proposals that we have in the budget.

STATE BLOCK-GRANT ADMINISTRATION

Senator RUDMAN. Mr. Kelso, as is our practice, if members of your panel or other members of your staff wish to answer to provide us with information, we would appreciate it.

One of the concerns that has been expressed by many, not just in this area, but other areas as well, is that when we get into the grants themselves you are going to start having all sorts of administrative layers set up which will be created at the expense of delivery of services at the local levels. What are you doing to prevent that?

Mr. KELSO. In both of the block grants—the maternal and child health that was effected in 1982 and the primary care that we propose to go into effect in 1983—the concept has been to provide the States with as much administrative and managerial flexibility as possible, so that the decisions can be made by the States on the utilization of the money.

We do not see that we would be a layer between the Federal Government and the States.

Senator RUDMAN. I don't think that you would be. We are concerned that some of these funds will not be used to provide essential services. They will be provided in many cases to expand and sustain bureaucracy that already exists.

Mr. KELSO. Our experience to date with the maternal and child health block grant indicates that States are eager to take over the maternal and child health programs, and the takeover is going very well. The MCH program was formerly operated under a formula grant. We anticipate that all 50 States, and 5 of the 7 jurisdictions will have taken over the block grants by the end of fiscal year 1982, and we believe they are doing a very commendable job. It is our view that they are not interposing any layers within the States.

Senator RUDMAN. I take it that you would not have an objection to report or bill language that would in some way develop a workable formula to assure that a high percentage of the funds that are going to be appropriated are used for the delivery of services?

Mr. KELSO. Mr. Chairman, we currently are looking at an allocation formula which probably will change the allocation process.

Dr. MARTIN. I think the question of the State administrative overhead is one that should be viewed in the context of the whole set of proposals of the new federalism. The question of directing the States to spend specified amounts for particular activities, I think, is one that the administration is actively discussing and generally opposed to. In MCH, while there have clearly been some administrative problems in States adapting to substantial internal constraints imposed by the States in terms of the number of employees, hiring freezes, and ceilings, these factors coupled with the substantial increase of flexibility associated with a reduction in our regulatory role, has resulted, if anything, in a decreased administrative burden at the State level on the local service delivery.

Speaking in a general sense, it would be difficult to take a position that would give less flexibility to the States. When the centerpiece of the block-grant concept is the shifting of control over and flexibility with the use of resources to the States. I would presume the administration would view that language as an inappropriate constraint on how the States could use the money.

Senator RUDMAN. I am particularly interested in your own experience with these programs in working with the States. Do you feel that in some instances they, in fact, do have more administrative costs than they should?

Dr. MARTIN. In administering the maternal and child health programs, State governments have historically had a substantially smaller administrative staff and professional staff at the State level, than was preferred by Federal administrators in previous years. There has been no apparent increase of those staffs.

I would say that, particularly under title V, there is a fairly lean staff of administrative and professional people in almost all States. There is invariably an exception, but even in those exceptions, like the District of Columbia, the overhead is not really related to the block grant. Title V overhead staff within the District of Columbia, although larger proportionate to population, is probably barely adequate.

MATERNAL AND CHILD HEALTH BLOCK GRANT

Senator RUDMAN. Can you tell us why the States of New York and California have not assumed operation of their MCH block grant?

Dr. MARTIN. In the case of California, I think the reason has to do with the particular budget process that the State of California goes through, both for their own State-appropriated funds and for the Federal funds, which requires a special legislative session during the spring. It is our understanding that California will be assuming operation of the block grant in the fourth quarter of this year.

The reason for New York, I think, had to do with a concern on the part of the State legislature and the Governor's office with regard to the matching requirement. It is our understanding that New York will be in on July 1. As with the State of New Hampshire, which had a comparable legislative difficulty in the first quarter, the problems in California and New York have been resolved and they are intending to come in this year.

Mr. KELSO. When I said 50 States, I assumed that California and New York would begin administering the block grants later this fiscal year.

SERVICES FOR WOMEN, INFANTS, AND CHILDREN BLOCK GRANT

Senator RUDMAN. Let's move on to several other programs. Can you explain why the administration is proposing a reduction, about 30 percent, in the WIC program and the supplemental food programs in light of the fact that all of the studies we have seen indicate that they are highly successful and very cost effective.

Mr. ITTEILAG. Mr. Chairman, the amount set aside in the budget for the WIC program came out of discussions that we understand occurred between the Office of Management and Budget and the Department of Agriculture. And we were not a party to those discussions.

So it is difficult for us to be specific about the rationale for the reductions. It is clear that some part of the reduction is envisioned as being accomplished through the reduction of administrative costs at both the Federal and State levels. But that clearly would not be sufficient to make up for the total decrease.

Senator RUDMAN. Do you have someone here from the Department of Agriculture?

Mr. KELSO. Yes; Mr. Bode.

Senator RUDMAN. Fine; then why doesn't he come up to the witness table.

Mr. BODE. The reduction in proposed funding for the special supplemental feeding program for women, infants, and children is based primarily on the intention of the administration to accomplish better targeting of benefits, delivered through the WIC program. I believe the cost effectiveness studies to which you referred are based on findings with newborns and do not necessarily apply to other participants.

So, I think better targeting is the means that will continue the programs most positive accomplishments at a lower funding level.

Senator RUDMAN. I hear your answer, but I want to pursue it. The difference in moneys you were talking about is substantial. If you look at the Harvard study, which of course I have been referring to and you have just responded to, it indicated a result of roughly $3 of savings in hospitalization costs for every $1 for pregnant women and newborn children. It seems to me that is a very cost-effective program. We may save it here, but we will spend it over there.

Dr. MARTIN. Senator Rudman, part of the response has to do with looking at that study in the context of the impact of supplemental feeding for pregnant women. As of October 1981, there were 2.5 million participants in the program. The study basically was consistent with findings with respect to those 437,000 recipients who were expectant and breast-feeding mothers. There is no question that for pregnant women and for infants, particularly in the first 30 to 90 days, insofar as their survival is based on the mother's nutrition, the WIC program has been very successful.

However, I think you cannot make the same kind of definitive argument for the other 1.5 million children in the program. It is my understanding, from talking to a number of health professionals in the States, that there would be a clear tendency to specifically target the funds available to expectant mothers since the research data show substantial medical and prenatal improvements in morbidity and mortality among the recipients. The reduction certainly would not have to cut into that population where there are research data to show that expenditures are useful.

Senator RUDMAN. What would the alternatives be for that part of the population that in fact is affected, the part of the population that you are not directing your targeting to? Where will these people receive nutritional benefits that I think many people feel they need? The food stamp program?

Mr. BODE. Certainly, those people will still be eligible to receive benefits through the food stamp program. I would also like to add, Senator, that the test applied in determining eligibility of the WIC program is administered by competent health professionals to determine whether or not the applicant is at nutritional risk. That is a relative factor. So, there at the administering level a determination is made and priorities are recognized. Those with the greatest need will continue to receive benefits.

PRIMARY CARE BLOCK GRANT

Senator RUDMAN. We will be very interested to see that. I have had a number of conversations with people in my State and people in other States in the New England area who have great concern about this particular program being cut back. If there are supplies from other programs that will meet the needs of these people, that is fine. But I think it would be tragic if some of the people who, in fact, have benefited from this program do not benefit, particularly amongst, in my State, the rural poor, of which there are many.

I want to move on to the primary care block grant. I note you are proposing to enlarge that primary care block grant. I would like you to explain why.

Mr. KELSO. Senator, our proposal to include categorical programs in block grants is part of the new federalism. This is essentially what the President asked for last year, and we believe that the proposal is consistent with the administration's policy.

FAMILY PLANNING

Senator RUDMAN. Do you subscribe to including family planning in that block personally?

Mr. KELSO. Mr. Chairman, my own personal view is that it could be done either way.

Senator RUDMAN. Don't you think it is likely that States, with their special responsibilities and budgetary constraints, are more apt to use the block for other things—community health centers and other community health services that the block can be properly used for—thus essentially reducing the amount of money that is available for family planning?

Dr. MARTIN. No, sir; as a matter of fact, I think the converse is true. In point of fact, almost every State has a major effort underway in family planning. Twenty-seven States and the District of Columbia have a single statewide grantee for the entire family planning program. By the end of the year we anticipate that 34 States will have family planning grants. Additionally, States have already, through State appropriations and title XX money, spent significant resources on family planning.

On the other hand, not very many States have as visible or as clear a role in primary care, and I would think, if anything, that States, faced with high-risk populations in regard to family planning services, would probably consider primary care dollars as being a lower priority for community health centers than for preventive services for high-risk women.

PRIMARY CARE BLOCK GRANT

Senator RUDMAN. We can only look at the track record, although to some extent maybe not strictly comparable, but fiscal year 1981 family planning had $162 million, down to $124 million in 1982. Now we are blocking it. I do not know what that will amount to under the block, but it is certainly an area that in many ways impinges on so many other areas of Federal Government with a proven case, particularly in certain concentrated population areas of the country, in fact, in rural areas as well, where family planning has had some very definite sound results.

Again, we, of course, do not know how this will turn out, but I expect we will want to know what this program goes through and exactly how much of the resources are allocated to family planning from this block. It will be interesting to compare it to the trend line that we have established over the last 2 years.

Let's look at the general development block grants.

First, how many States have applied for planning grants, to your knowledge, at this time to assist them in preparing to assume responsibility?

Mr. KELSO. Thirty-five States have expressed an interest in receiving the planning grants.

Senator RUDMAN. To what extent are you presently evaluating State performance under the block grants?

Mr. KELSO. We have corresponded with Governors, State health officers, and medical societies, asking for their comments and their opinions on community health centers. We have, throughout this fiscal year, reviewed and evaluated the community health centers to be sure that the best ones will be turned over to the States in 1983.

We have worked very closely with the States on the community health centers. As a matter of fact, we have developed two cooperative agreements, one with the State of West Virginia and one with the State of Kentucky.

BUREAU OF COMMUNITY HEALTH SERVICES PROGRAM SUPPORT

Senator RUDMAN. What percentage of your employees previously involved in migrant health and family planning categorical programs will be retained to help administer the primary care block grant?

Mr. KELSO. The Bureau of Community Health Services, if all our proposals are implemented, would have 121 positions in 1983.

Dr. MARTIN. If you are referring to fiscal year 1982, within the central office, the effect of the reduction in positions was largely on nonprogrammatic staffs.

Insofar as the Office of Family Planning, the Office of Maternal and Child Health, and the Office of Primary Care are concerned, with few exceptions, which had to do with the RIF register, nearly all staff have been retained. The same is true in the regional offices.

For fiscal year 1982, both for the MCH block, which has been implemented, and for the primary care block, which is in the process of being developed, the preponderant numbers of staff whom we have in program areas have been retained. The 150- to 200-position reduction we have taken has been due largely to retirements and normal attrition in support divisions, as opposed to programmatic staff. There are exceptions. But in general, the staff who remain are clearly knowledgeable about the programs.

MATERNAL AND CHILD HEALTH SET-ASIDE

Senator RUDMAN. Moving on to another subject within the same grant, what provisions are being made for provision of services for mentally retarded persons under the MCH block grant?

Dr. MARTIN. There are two components in the report of intended expenditures submitted by the 53 States and jurisdictions that have already received money for the block. A majority of those States clearly identified mental retardation and rehabilitative resources for children as a high priority.

In addition, in the consolidated Federal component—the MCH 15-percent set-aside—there is a clear priority for the special programs for the mentally retarded at university-affiliated facilities.

ADOLESCENT HEALTH

Senator RUDMAN. This grant includes authority to provide the services designed, amongst others, to prevent the first of repeat pregnancies in adolescents. Since this authority continues, explain, if you will, to the committee the need for a separate categorical program such as adolescent family life.

Dr. MARTIN. The previous program, the adolescent health program, was incorporated into the consolidated Federal and State effort under the title V block. That program dealt with a broad range of concerns associated with adolescent health, lifestyles, and the like. It is, in fact, now incorporated into the block, even though those grantees are still categorical through September.

The administration feels that there are a number of specific public health problems, for which there needs to be a targeted activity. Immunizations is one example. Adolescent pregnancy and family life activities are very high priorities with the administration. And it is felt that the best way to carry out research and demonstration activities is a targeted approach.

COMMUNITY HEALTH CENTERS

Senator RUDMAN. Moving on to community health centers, I wonder if you could tell me—give me an estimate of how many will have to close or reduce their services substantially because of the impact of the budgetary reductions and also how many will be closing because they failed to meet criteria for management efficiency under the new law?

Mr. KELSO. During 1982, approximately 200 centers will not be refunded.

Senator RUDMAN. How many?

Mr. KELSO. 200.

Senator RUDMAN. Out of how many?

Mr. KELSO. 872.

Senator RUDMAN. About a quarter of them will not be?

Mr. KELSO. That's right.

Another 200 centers will receive only 90 to 100 percent funding—in other words, not complete funding. And another 450 centers will be funded at levels significantly less than they received in 1981.

Senator RUDMAN. What is the outlook for those that will have that significant reduction as far as their continued ability to operate?

Mr. KELSO. Some of these centers are able to continue without Federal support.

Dr. MARTIN. Without regard to the 450 centers with reduced funding, the level of reduced funding is carefully designed and negotiated with the grantees, such that we have every expectation they will continue to deliver services. And a lot of those cuts are made in areas like hospitalization, supplemental services, and also are related to increases in third-party reimbursements and improving efficiency.

No center that we funded this year will be funded at a level that will make it impossible to continue delivering services. There will be 200 centers that receive phaseout funding and discontinued Federal support. About 60 percent of those will continue to deliver services without Federal grant dollars.

Senator RUDMAN. What about the 40 percent? What about the 80 that cannot?

Dr. MARTIN. They will close.

Senator RUDMAN. Will that leave a need in some of those communities?

Dr. MARTIN. The basis for defunding has to do largely with the congressional directive on need and demand. For example, for a center in downtown Honolulu, Hawaii, it is fair to assume that there are alternative resources within that community. We are not closing one down in the middle of Watts. As part of our congressional mandate, we are determining whether alternative services and other providers are available in the community and whether the community is capable of assuming responsibility for those patients.

In our judgment, the bulk of the patients who are no longer served by these particular centers can find alternatives. And the centers where there are no alternatives are the ones that we plan to continue to fund, like Watts and South Bronx.

PRIMARY CARE RESEARCH AND DEMONSTRATION

Senator RUDMAN. I am sure that you're aware that the Reconciliation Act, which you were just talking about in relation to your last comment, also omitted the provision authorizing funding of rural projects under the primary care research and demonstration program.

Can you tell us what you may be doing to see that necessary legislative direction is made to permit the program to be phased out in an orderly manner?

Dr. MARTIN. The Secretary is responding to a letter from Senators Hatch and Kennedy and Congressmen Waxman and Madigan in which they requested that no policy or program decision be made that would jeopardize those programs pending the introduction of conforming technical changes that would correct that particular section of the act. The Secretary is responding affirmatively, and we shall do everything we can, pending receipt of that particular technical amendment, to assure that those particular programs do not go out of business.

The money has not been spent. We have until June to spend the $1.9 million.

Senator RUDMAN. Do you know if the letter from the Secretary has been sent to the various committee chairmen, those in the House?

Mr. ITTEILAG. I do not know.

Mr. LITTLE. We know that a letter has been sent to the Department.

Senator RUDMAN. Would you, for the record, supply this committee with a copy of that letter when it is sent?

Mr. ITTEILAG. Mr. Chairman, I will inform Mr. Kaganowich as to its exact status.

FAMILY PLANNING

Senator RUDMAN. We are very interested in that. A number of the members of the subcommittee are. We would like to see that as soon as it is drafted and sent.

I want to move on to the 1981 General Accounting Office report which identifies several areas in which improvements in title X management to reduce programs costs can be made.

You are familiar with what that report recommended. What action have you taken in response to that GAO report?

Dr. MARTIN. The major cost-saving recommendations were the first two recommendations in the GAO report. The first one recommended that we modify our guidelines to reflect changes in the state of the art for family planning services with regard to visits and consultation. Those particular changes have been made in consultation with the American College of Obstetricians and Gynecologists, have been communicated to all of our programs in the field, and have been implemented.

The second recommendation had to do with establishing more appropriate fee scales in order to assure increases in third-party reimbursements. There are two parts to what the Department has done: The fee scales and the collection of third-party receipts by those grantees. There has been substantial improvement and great emphasis placed on the collection of funds in the program.

With regard to the former, one of the changes being recommended in the recently published regulations concerning family involvement is to no longer consider adolescents' financial status based simply on their own incomes. There are about 1.2 million users of that particular system. New regulations propose that, for adolescents, the available family income be used as the basis for charging fees. That should substantially increase the third-party and individually reimbursable charges from title X agencies, particularly where there are large numbers of adolescent users.

As for the other two recommendations, one had to do with the reporting system to be utilized in the development of the new reporting system. The Department did not concur with that recommendation. It is particularly inappropriate with the proposal of the block grant and, in fact, would cost significant additional money.

The other recommendation had to do with modifications in title XX. Title XX is now a part of a block grant to States. The Department nonconcurred with that recommendation because it feels it is inappropriate to impose sliding fee scale requirements on State governments.

Senator RUDMAN. Do you happen to know statistically at this point what percentage of those recipients are paid in full, in part, or not at all?

Dr. MARTIN. We don't collect that data, but we can provide information on sources of revenue for all users of family planning services, expressed by percentages.

Senator RUDMAN. Would you do that, please.

Dr. MARTIN. Yes.

[The information follows:]

Sources of revenue for family planning services—Calendar year 1980

	Percent		Percent
Title X	49	State	7
Title V	2	Local	4
Title XIX	6	Other	4
Title XX	13	Noncash donations	7
Other third-party payments	1		
Patient fees	7	Total	100

REDUCTION IN SCHOLARSHIP-ASSIGNEE PAY

Senator RUDMAN. Your budget requests elimination of the special retention bonus for those fulfilling their obligation for service in the National Health Service Corps. It would save for each commissioned officer about $9,000. What will the effect of this be on morale, productivity, and other effects on those who lose this payment?

Mr. KELSO. The reason for the special retention pay was to retain career commissioned officers in the Public Health Service. These individuals who serve in the National Health Service Corps have been the recipients of National Health Service Corps scholarships to support their medical school training. They then become obligated to serve with the National Health Service Corps in shortage areas. We feel that providing them special retention pay is not appropriate because they are obligated to serve.

Senator RUDMAN. You do not think there will be any special problems where you have two categories both doing the same approximate jobs, one group receiving——

Mr. KELSO. The reduction will be applied across the board, beginning in 1983, for those newly entering or renewing obligated service agreements in the corps.

Senator RUDMAN. The committee was told that those who do not have a service obligation will be receiving one amount and those who do another amount. Is that untrue?

Mr. KELSO. A regular commissioned officer in the U.S. Public Health Service would receive the special retention pay. But an obligated individual serving in the National Health Service Corps would not receive the special retention pay beginning in 1983.

Senator RUDMAN. And that doesn't have any effect on morale?

Mr. KELSO. I am sure that those who are obligated and currently are receiving the special pay would like to continue, but the reason for the special retention provision was to retain career officers who did not have to serve obligated duty.

Senator RUDMAN. I understand what you are saying. I understand it very clearly.

How many people are involved here?

Mr. KELSO. 330 commissioned officers.

Senator RUDMAN. I really think that answers my question. I am not sure that that really is the kind of saving that would be worthwhile given the problems that I expect you will have. Those are your problems and not mine.

Mr. ITTEILAG. Mr. Chairman, there might already be a problem of morale in the sense that some who are serving who received scholarship support over a period of years have gotten what amounts to a free education at the courtesy of the taxpayers. So, I think it is an attempt to provide a certain amount of equity in that regard.

EXCEPTIONAL FINANCIAL NEED SCHOLARSHIPS

Senator RUDMAN. According to figures I have seen recently, a lot of people have received an education at the expense of the taxpayers. Under health professions student loans, 167,000 doctors received loans and 55,000 are now in default, either fully or seriously. This is another program. As far as the Government paying for education, it has paid for many that it intended to and many it did not intend to.

I just raise my point that I am not sure, with the number of people involved, that is necessarily and efficacious practice in terms of saving money, in terms of what it might cost. As I said, it is really your problem, not ours.

I want to turn to an exceptional need scholarship. According to some studies, we face a surplus of 70,000 physicians by 1990. Why should the Federal Government continue to sponsor the exceptional needs scholarship program?

Mr. KELSO. We are not asking for any funds in 1983 for the EFN program.

Senator RUDMAN. But the revolving fund will continue to fund the people under that program.

Dr. WHITESIDE. The health professions revolving fund is a loan fund from which former EFN students can borrow. The EFN program has, in the past, only supported the student during the first year of the individual's training. And those people could borrow from the revolving fund to complete their education.

Senator RUDMAN. Just to complete?

Mr. KELSO. Yes.

LOAN DEFAULTS

Senator RUDMAN. The health professional student loan program was the subject, of course, of the Inspector General's report that showed substantial delinquencies in repayment of loans. What are you doing about that?

Mr. KELSO. The Inspector General looked at 24 different institutions, and found 2 problem areas. The first was with due diligence, which is the degree to which the institutions were actively trying to obtain repayment of the loans that had been made. The other area of concern was with the excess money in the revolving fund that was not being used to make loans.

We have provided copies of this report to the institutions, and we have instituted followup procedures. We have established standardized delinquency rates, and we have asked for reports from the institutions on how well they are doing in implementing improvements in their debt management efforts.

Senator RUDMAN. Isn't it true that one of the items within the report indicated—it caught my eye because one of the institutions is in my State—those institutions that had a very solid program of exit interviews with those graduates to discuss how they would repay, and what their obligations were, had a considerably lower default rate. In fact, Dartmouth College Medical School had a rate of about 3 to 3½ percent, which was about one-sixth or one-seventh of the national average.

Would it not seem that this might be a requirement imposed on these institutions to insure that people are informed of their responsibilities? Certainly it would seem that any profession which, as of last week, was rated as the highest paid profession in America—that there is just something scandalous about 50,000 to 55,000 practicing physicians across this country, having fully participated in the program, being either in serious default or being very delinquent.

I just wonder whether or not there ought to be a more vigorous approach taken to make sure that these funds are collected and collected properly.

Mr. KELSO. We subscribe to a more vigorous approach. The exit interview with a student to explain their loan repayment obligations would be helpful.

We are concerned about the delinquency situation, and debt collection is one of our high-priority activities for the current and next fiscal years.

Senator RUDMAN. I just want to point out to you, there was one short paragraph within the GAO statement which, Mr. Kelso, I just think is worth repeating here. I appreciate the testimony; I expect you will do precisely what you say, but let me point out that the GAO said that:

> In addition, we found that HSA had not effectively monitored either the institutions' collection activities or their accumulation of large amounts of cash. Further, agency accounting records for the program were not reliable. At best, the agency made only token efforts to control the funds for the two programs.

You may dispute that paragraph. It certainly seems to me that there is a long way to go from that statement to where we are today, to insure that taxpayers are given a fair shake in making sure that their money is properly used.

Mr. KELSO. We do not deny that we have a problem. We certainly do, and we plan to allocate considerable resources to solve the problem.

USE OF COMMERCIAL COLLECTION AGENCIES

Senator RUDMAN. Tell me, have there been any thoughts given to turning some of these delinquent accounts over to normal commercial collection agencies?

Mr. KELSO. Yes, sir; we have a contract activity in process to deal with repayments under the HEAL program. In addition, we are encouraging the schools to contract with collection agencies to assist in their collection efforts.

Senator RUDMAN. Let me simply say to you that out there in the real world—I always make this statement when I'm here in Washington—out there in the real world a physician who is practicing medicine in my hometown, who suddenly is contacted by a local credit collection agency which notes that he is driving two luxury cars and living in an expensive home, and living the good life, that he is *x* number of dollars in default to the Federal Government, and unless payment is made promptly, he will have attachments made against his home, his cars, and his various other assets. It is amazing how quickly that individual will respond with alacrity to that agency. As to what they will respond to when they get a letter from the Federal Government which promptly goes into the wastebasket——

So I hope you might respond to your contract bids promptly, and hopefully would have ongoing a vigorous collection system, so that next year when we sit down at this hearing, we can again review it and see what progress has been made.

Certainly, this isn't going to inspire the confidence of the American people, when a profession such as the medical profession stands out as a class probably more seriously in default on these loans than any other single group.

Mr. KELSO. There is a legislative proposal being reviewed at the Department which would give us more authority to handle debt collection. One of the provisions has to do with cooperative agreements with credit bureaus.

Senator RUDMAN. Staff counsel just passed me one section, which I had seen; I will quote it to you. It is illustrative; I am sure you have read it but in the event other things have occupied your mind:

> One borrower, delinquent for over 7 years on a student loan with a balance of $3,288, just obtained a loan of $220,000 to purchase a home.
>
> Another borrower, delinquent for over 3 years with a loan balance of $2,940, paid off two commercial loans for $13,000, was current at $56,000 to purchase real estate, and had a line of credit of over $7,000 with several banks and department stores.
>
> The third borrower, a health professional student, had a loan balance of $7,000, delinquent; he is current on a $25,000 loan on a home improvement.

I don't have to just go on and on and read you all these horror stories. There is no question at all that something has to be done. For 1982–83, the staff resources allocated to debt management will remain at 24 positions; is that correct?

Mr. KELSO. Yes, sir.

Senator RUDMAN. What do you intend to do? Essentially subcontract a lot of this out to a commercial agency and do it that way?

Dr. WHITESIDE. Yes; we plan to contract a lot of that work out. We would be contracting, for example, with collection agencies with respect to our HEAL program, as well as for monitoring of institutions that manage the health professions and nursing student loan moneys.

And we would hope to have a second contract to assist some institutions who seem to be having problems with their actual accounting of these funds.

We think these kinds of activities will greatly reduce the default rate in a relatively short period of time.

Senator RUDMAN. What kind of credit agencies are you dealing with to produce a contract? Are they major national agencies? Small, local agencies, State-based agencies?

Dr. WHITESIDE. We would like to have either an agency that is national or at least regional in scope, because we do have a fairly large problem.

Senator RUDMAN. There are those in the credit industry who tell us that this type of collection might be better served with small effective units that operate within various States rather than to go to a large national organization which, in many ways, may be more bureaucratic than the Government itself.

I would hope that whatever you do you choose the right one, because I can say this: That when we get back here next year, if we do not find much improvement in this, I think there are going to be some unhappy people on that side of the table as well as this. I would certainly hope that something is done about it.

It has been the subject of a lot of discussion and a lot of comment by individuals that I have talked to, who just do not understand how the Federal Government can allow this to go on.

Mr. KELSO. The Secretary is taking a very personal interest in this whole problem. He has had the Inspector General involved; he has talked to the General Counsel, and of course, he has us involved. It is one of the objectives that we are monitored on by the Secretary.

NURSING STUDENT ASSISTANCE

Senator RUDMAN. I think we can leave that and move on to nurses' training for just a moment.

The amount of student loan funds in that area declined from $22.3 million in fiscal year 1978 to $13.5 million in 1981, and half that for the current year. In fiscal year 1978, $8 million is awarded for nursing scholarships, but there are no funds in that program in 1981.

I am curious as to what the extent of delinquencies are in that particular program.

Dr. WHITESIDE. In the 20-percent range figure, it relates to both health professions and nursing combined. If you want to look just at nursing, 26 percent of the nursing borrowers are delinquent with respect to their repayments.

Senator RUDMAN. I assume you are approaching that in the same way?

Dr. WHITESIDE. Absolutely.

PUBLIC HEALTH SERVICE HOSPITALS AND CLINICS

Senator RUDMAN. Let's just move on for a moment, to Public Health Service hospitals. The current fiscal year, Congress provided $146 million for transferring eight Public Health Service hospitals to local or other sponsors.

Can you give us an update on where matters regarding these facilities presently stand?

Mr. KELSO. Yes, sir; all of the PHS hospitals and clinics were closed as Public Health Service facilities. Five of the hospitals—Boston, Baltimore, Seattle, Staten Island, and Nassau Bay, and five of the clinics, were converted to community-based organizations. In addition, San Francisco, Norfolk, New Orleans, and two clinics, Honolulu and St. Louis, were taken over by either other Federal or State entities.

Senator RUDMAN. I take it then that we are essentially now free of our obligations and other responsibilities regarding these hospitals?

Mr. KELSO. By the end of this fiscal year, we will be totally out of it.

HANSEN'S DISEASE

Senator RUDMAN. Can you tell us what arrangements were finally made for the treatment of leprosy patients who had been cared for at various PHS facilities other than Carville?

Mr. KELSO. We still have Carville; and we also have negotiated contracts around the country to take care of other individuals with Hansen's disease.

BUREAU OF COMMUNITY HEALTH SERVICES PROGRAM SUPPORT

Senator RUDMAN. Assuming that the President's legislative proposals were accepted unmodified by the Congress—I think it is unlikely, but assuming that, what resources would your budget request allow for the provision of technical assistance to the States during the transition of the large primary care block grant?

Mr. KELSO. The Bureau of Community Health Services would have 121 positions, and we would use many of those 121 positions to provide technical assistance.

SUBMITTED QUESTIONS

Senator RUDMAN. Mr. Kelso, we do have some additional questions, and I believe some other members of the Subcommittee will have some questions, which we will furnish you. If you would please provide the answers for the record.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

STATE BLOCK GRANT ADMINISTRATION

Question: We have been most concerned that the States implementing the block grants will use the funds to maintain layers of local administration at the expense of cutting back on providers and essential services. What instructions, if any, do you give the States to prevent the Bureaucrats from taking away service and provider money?

Answer: We are making every possible effort to reduce the number of requirements placed upon the States.

We are firmly convinced that we can rely on the States to manage their programs at least as efficiently and effectively as programs administered from the Federal level. We are hopeful that the consolidation of a number of categorical programs into a simplified block grant will encourage States to create an active planning process focusing on establishment of priorities; targeting of high risk patients; and better utilization of all Federal and State resources in order to assure that services are available to their most needy citizens. We believe that the States will combine services and organize them in ways that are best suited to meet the needs of their clients.

MATERNAL AND CHILD HEALTH BLOCK GRANT

Question: How many States assumed operation of their Maternal and Child Health (MCH) block grants on October 1?

Answer: Fifty-two States assumed operation of their Maternal and Child Health activities under the Block Grants as of October 1, 1982. By the end of fiscal year 1982, 56 of the 57 States and Territories are expected to be administering the MCH Block Grants.

Question: Describe activities that will be funded at Federal, State, and local levels under the MCH block grant.

Answer: Activities that will be funded at the State and local level are those directed to the reduction of infant mortality and the incidence of preventable disease and handicapping conditions among children. They include quality prenatal and perinatal care, immunizations, diagnostic and treatment services, pregnancy care, preventive services particularly for preschool and school-age children of low-income families, and hospitalization for high-risk mothers and children who are crippled or are suffering from conditions leading to crippling. Other services relate to children who are permanently disabled, families which have lost children due to sudden infant death syndrome, children suffering from lead-based paint poisoning and adolescent pregnancy preventive services.

At the Federal level during fiscal year 1982 we will administer the special projects of regional and national significance including those for research, training, genetic disease information and counselling, hemophilia centers, and pediatric pulmonary centers.

SERVICES FOR WOMEN, INFANTS AND CHILDREN BLOCK GRANT

Question: For fiscal year 1983, the Administration proposes to transfer responsibility for the Women, Infants and Children and Commodity Supplemental Food Programs from the Agriculture Department to the Department of Health and Human Services. Funding for the categorical programs proposed for consolidation would be decreased 30 percent below fiscal 1982 levels. What specific reductions in services will States have to make in the WIC and Commodity Supplemental Food programs as a result of funding decreases?

Answer: As the WIC and MCH programs are combined, we believe that significant economies will be made and that efficient means of identifying high risk and high need persons will be developed in the States. As a result, we expect that where WIC intervention is truly vital and/or of proven effectiveness, such as, with expectant and breast feeding mothers, there will continue to be full service to such clients.

Question: In shifting administration of these categorical programs into HHS, it would appear that the expertise and knowledge of the Agriculture staffs would be lost in the process. What steps do you propose to take to make certain the staff expertise follows the blocks if they are shifted?

Answer: Shifting the WIC program to HHS will not result in loss of expertise and knowledge since the program is already administered in the States by the State health agencies. In most States, the program is conducted by the MCH unit of the State health agency. Actually, the transfer of the program is expected to increase the efficiency of the operation.

Question: Do you propose to limit Federal reimbursement for State administrative expenses associated with operation of the WIC and Commodity Supplemental Food programs?

Answer: The detailed specifications for the Services for Women, Infants, and Children Block Grant are still being developed and no final decision has been made with regard to Federal reimbursement for State administrative expenses. However, one of the principles that guides us in drafting specifications for the block grant is the need to avoid imposing requirements upon the States. Indeed, one of the reasons for the consolidation of the MCH and WIC programs is to reduce the administrative cost burden for the States by combining the administrative components of the two programs.

PRIMARY CARE BLOCK GRANT

Question: We note you are proposing an enlarged Primary Care Block Grant in fiscal 1983. What is the reason for this proposal?

Answer: It was the Administration's intention to identify similar and related activities and combine them into block grants, thereby shifting decision making responsibilities to the States and enabling them to be flexible in attacking problems found within their borders.

Question: Why include Family Planning in the block?

Answer: Family planning is an integral aspect of primary care and the program is managed in a manner comparable to that of other programs included in the Primary Care Block Grant; therefore, it is logical that it be included in this activity. We feel that this combination will permit the States to do a more efficient, effective job of planning and coordinating their own service programs, establishing priorities and allocating resources to the most urgent areas of need.

Question: What accounts for the $4 million increase you propose in the money available to the block over comparable amounts for fiscal year 1982 for the individual programs involved?

Answer: The increase of $4 million in fiscal year 1983 will restore the program to the 1982 Continuing Resolution level before the administrative reductions and requested reprogramming for pay raise were made in the current fiscal year 1982 request.

BLOCK GRANTS

Question: We are concerned about the development of the block grants under your agency and have a number of questions about this. How many States have applied for planning grants to assist them in preparing to assume responsibility for the Primary Care Block Grant?

Answer: Thirty-five States have expressed an interest in receiving the planning grants. Because no funds have been available for planning grants, we have not formally solicited proposals.

Question: To what extent are the States complying with the requirement that they spend specific sums for certain activities under the MCH block?

Answer: It is too early to know the amounts being spent by States pursuant to Sec. 505(2)(C)(i) of the statute which requires that "the States will use a substantial proportion of the sums expended by the States for carrying out this title for the provision of health services to mothers and children with special consideration given, where appropriate, to the continuation of the funding of special projects in the State previously funded under this title...." In a review of the Reports of Intended Expenditures and Statements of Assurances it was found that only one State indicated that several special projects would not be funded when the block grant is implemented. Each State is required by law to prepare and submit an annual report of its activities under the block grant.

Question: How much money will you save over 1982 levels through the consolidation of additional categorical programs into the Maternal and Child Health and Primary Care Block Grants?

Answer: Funding requested for the Primary Care Block Grant in 1983 is the same as the 1982 Continuing Resolution level. The SWIC Block Grant would sustain a reduction of $281.5 million from the 1982 comparable levels. In addition, program support would be reduced by 443 positions and $16.2 million, of which, 304 positions and $11.7 million are associated with the block grant consolidation. Also, a number of Program Management positions and related dollars would be eliminated as a result of these proposals. We expect, however, that through increased efficiency and the reduction of Federal requirements under the block grant, the States will significantly reduce the amount of grant funds which are spent on administration.

Question: Why does the Administration support legislation that would remove limitations on administrative costs, matching requirements and transfer of funds and other provisions that serve to protect the integrity of the MCH and Primary Care Block Grants?

Answer: The current Primary Care Block Grant legislation poses certain barriers to effective implementation of the block grant program by the States. We believe that, if these barriers were removed, many of the States would accept the block grant in fiscal year 1983 and the remainder would assume responsibility for the Primary Care Block Grant in 1984. Without the amendments, conversion to block grants will be slow with only a limited number of States participating.

The changes we propose are: to reduce the matching requirement; to allow block grant funds to be used for State administrative costs; to relax the maintenance of effort requirement for existing grants; and to remove the required adherence to legislative requirements for service levels and governance for block grants to States.

We believe that these changes will not hurt the integrity of the block grant program. Discussions with the States indicate they are aware that acceptance of the block grant carries with it a responsibility to address the issue of allocating health resources.

Most States are aware that ambulatory care, when made accessible, can help reduce the need for more expensive care such as inpatient health services.

State responsibility along with periodic audits and GAO monitoring will be sufficient to maintain the integrity of the program.

MATERNAL AND CHILD HEALTH SET-ASIDE

Question: The Statute establishing the Maternal and Child Health block grant authorizes the Secretary to set-aside 15 percent of the total appropriation in fiscal year 1982, and between 10-15 percent in other years, for demonstrations, research, training, hemophilia projects and other related activities. What percent of your fiscal 1982 allocation was set-aside for discretionary activities?

Answer: Fifteen percent of the total MCH Block Grant funds, a total of $52.1 million, was set aside in fiscal year 1982 for special projects of regional and national significance.

Question: What kinds of activities have you funded?

Answer: The activities funded under this set-aside include: University Affiliated Facilities; adolescent health; Pediatric Pulmonary Centers; genetic services; hemophilia centers; biochemical/cytogenetic laboratories; schools of public health; unidisciplinary professional training projects; orthotic and prosthetic services; applied research; improved pregnancy outcome projects; improved child health projects; child development centers; and a variety of special demonstration projects.

ADOLESCENT HEALTH

Question: The MCH Block Grant includes authority to provide services designed, among other matters, to prevent the first or repeat pregnancies among adolescents. What can you tell us about State interest in this part of the Block Grant? What are the States doing?

Answer: States are required by statute to describe the intended use of funds received under the MCH Block Grant. During the fiscal year 1982 transition period, programs will be tailored to the needs the States elect to address. The Block Grant concept allows each State to determine the specific needs of its population. Reports of intended expenditures submitted by States in their application for fiscal year 1982 block funds were general in nature, and did not address specific program components such as adolescent pregnancy. Categorical Adolescent Pregnancy Prevention Programs were funded late in fiscal year 1981 for operation during fiscal year 1982.

Question: If there is a point to have a separate program, why not include a set-aside within the Block to assure that all States provide services to adolescent women?

Answer: The States are continuing to deliver essential maternal and child health services and services to handicapped children. We expect that under the MCH Block Grant they will provide services to adolescent women where that is determined to be a priority by the State. The Adolescent Family Life Program, however, is a demonstration program aimed at identifying effective means of both preventing early pregnancy and caring for already pregnant adolescents and young parents. It is designed to examine the effectiveness of a variety of activities in providing services to adolescent women. We would hope States would consider replicating those which are identified as effective, within their activities supported with block grant or other funds.

COMMUNITY HEALTH CENTERS

Question: To what extent will any Community Health Centers have to be closed or have their services cut back because of the impact of budget reductions or because they fail to meet criteria for management efficiency in the new law?

Answer: So far about 129 grants have been phased out and we expect that, by the end of September 1982, we shall have a total of 200 which will no longer be dependent on Federal funding. Sixty percent of these are expected to continue in operation using other funding sources.

Question: How many Community Health Centers will the Primary Care Block Grant be supporting in the future?

Answer: We expect that, by the end of fiscal year 1982, there will be 672 CHCs still receiving Federal support. In those States which initiate Block Grant operation, continuation determinations will reside with them. Because of our intensive efforts to identify and support most needed and most effective centers, we are hopeful that a great majority of centers will be continued.

Question: Are new standards for administrative or clinical performance being developed? What's happening?

Answer: No new standards are being developed. We have, for several years, employed standards having to do with provider productivity, administrative costs, financial management, and costs per medical encounter. We have also employed clinical standards which emphasize the importance of preventive measures, for example, immunizations, hypertension screening, pap smears and the like. We are providing information on these standards to the States as well as information on the associated monitoring systems for their consideration and utilization as they see fit.

PRIMARY CARE RESEARCH AND DEMONSTRATION

Question: We know you are aware that the Reconciliation Act omitted a provision authorizing funding rural projects under the Primary Care Research and Demonstration program. Will the funds provided in fiscal 1982 be sufficient to phase out the program--or will additional funds be needed in fiscal 1983?

Answer: On December 21 we received a letter signed by Congressmen Waxman and Madigan and Senators Hatch and Kennedy advising of their intent to introduce technical amendments into legislation which would authorize grants to Primary Care Research and Development projects serving both rural and urban areas. We support the intent of the technical amendments and have prepared a response indicating that support.

Assuming that corrective action is taken in time, we plan to spend $1.9 million on the Section 340 program in 1982. Approximately 15 projects will be funded in fiscal year 1982. The authority for this program expires in 1982 and it is not anticipated that additional funding will be required in 1983.

Question: What is the status of the CARES program in North Dakota? How long will it continue to be funded?

Answer: The CARES, North Dakota project, is currently viable. It is supported by a Primary Care Research and Demonstration grant through September 30. The CARES project, as well as all other continuation projects, is eligible to compete for 1982 funds.

FAMILY PLANNING

Question: A 1981 General Accounting Office report identified several areas in which improvements in Title X management could reduce programs costs and enhance program effectiveness. For example, the report stressed fewer routine clinic visits, matching client education with client needs, and conducting only those laboratory tests that are medically necessary or justified by local conditions. What data collection and program monitoring efforts are performed under Title X to evaluate program effectiveness?

Answer: The Bureau of Community Health Services has in operation a uniform reporting system entitled "BCHS Common Reporting Requirements." Information submitted in accord with the BCRR is used to assess managerial and clinical effectiveness of grantees and among other things, can measure the number of encounters, medical and other, the number of users, and the costs associated with these by tracking ratios of encounters to users; medical versus total costs per user and encounter; and administrative costs. Over time we can identify changes in effectiveness and efficiency that bear closer accounting through regional site visits, technical assistance reports, financial reports, and audits. All of these mechanisms are used to manage and evaluate effectiveness.

Question: Can you describe the findings of Title X evaluations conducted to indicate progress made by the program in preventing unwanted pregnancies?

Answer: The program has not conducted evaluations specifically looking at its progress in preventing unwanted pregnancies. Federally supported studies conducted under the auspices of the National Institute for Child Health and Human Development have examined adolescent sexual behavior, the use of contraception and the impact of family planning programs on adolescent pregnancy. The most significant research has been done by Melvin Zelnik and John Kantner, et. al., of the Johns Hopkins University. The following statistics have been reported:

One in five females has had intercourse by age 16 and two-thirds by age 19, almost all of which experience is premarital. One in 10 U.S. women becomes pregnant before age 17 and one in four before age 19; 8 in 10 of these pregnancies are premarital. More than one-third of those who are sexually active premaritally have a premarital pregnancy before age 18, one-fourth by age 17.

Between 1971 and 1976, the number of repeat pregnancies among teenagers who had had a premarital first pregnancy fell substantially, suggesting improved contraceptive usage. Among those who stayed unmarried after the first pregnancy outcome, declines were notable among whites, younger teens and those whose first pregnancies ended in abortion.

About 780,000 teens experience premarital pregnancy each year. It is estimated that an additional 680,000 would become pregnant if they were not effectively using contraception.

Another federally supported study by Jacqueline Darrah Forrest of the Alan Guttmacher Institute and Albert I. Hermalin and Stanley K. Henshaw of the Population Studies Center of the University of Michigan reported that during the 1970s, an estimated 2.6 million unintended pregnancies were averted among teenagers as a result of their enrollment in family planning clinics. Nearly one million unplanned births and 1.4 million abortions were prevented. In 1979 alone, 417,000 teen pregnancies were averted.

Question: The Subcommittee is also concerned that family planning clinics pay their way, to the extent possible. For example, there should be a consistent and fair policy regarding payment and levels of payment. How much money will Title X clinics collect from third-party payers during fiscal year 1981 for family planning services and how does this compare with previous years? What about 1982?

Answer: It is estimated that Title X clinics collected about $78 million in third-party payments in 1981. The increase in third-party payments to family planning clinics has been gradual over the years. In 1974, third-party payments totalled about $27.3 million. By fiscal year 1977, payments under Titles XIX and XX had increased to $71.9 million. Third-party payments in 1980 totalled about $78 million, the same amount as estimated for 1981. It is not possible to project family planning third-party payments for 1982. The Social Service Program, Title XX, under the block grant legislation, is administered by the States at reduced appropriation levels. Since the intent is to give the States as much flexibility as feasible, family planning is no longer identified as a required service under this program. While Medicaid, Title XIX, was not changed administratively, caps will restrict expenditures to about $55,000,000, the same amount as estimated for 1981.

EXCEPTIONAL FINANCIAL NEED SCHOLARSHIPS

Question: Why shouldn't those who receive Exceptional Financial Need (EFN) scholarships be required, in turn, to give service later in medically underserved rural areas?

Answer: The purpose of the Exceptional Financial Need Scholarship program is to enable students with exceptional financial need to concentrate fully on curricular endeavors without fear of financial distress and without incurring a service commitment during the early stages of their medical education. It is assumed that once students have completed the first year of study they are in a better position to make a realistic choice between accepting a loan, a service-conditional scholarship, or some other form of financial assistance. In the past, some EFN recipients have applied for and received priority consideration for National Health Service Corps (NHSC) continuation scholarships which, of course, obligates them to serve in health manpower shortage areas.

HEALTH PROFESSIONS STUDENT LOANS

Question: The Health Professions Student Loan program was the subject of an HHS Inspector General's report that showed substantial delinquencies in repayment of loans. Delinquencies apparently run into the millions.

Why did HHS allow this situation to develop? Lack of authority? Lack of staff? Laxity?

Answer: The main objective of the Health Professions Student Loan program has been to make loans to as many needy students as possible. Emphasis has recently been placed on debt management and collection. We have initiated a number of activities at the Federal level and within the institutions which will result in lower delinquency rates in the future.

NURSING STUDENT LOANS AND SCHOLARSHIPS

Question: The amount of student loan funds awarded to programs for nurse training has declined from $22.3 million in FY 1978 to $13.5 million in FY 1981 and about half that in the current fiscal year. Eight million dollars were awarded in FY 1978 for nursing scholarships but no funds were awarded for the program in FY 1981.

What percentage of nursing students have been receiving nursing student loans and scholarships?

Answer: It was estimated that in academic year 1980-81 approximately 14 percent of the eligible enrollment of nursing schools received Nursing Student Loans (including loans made from the revolving funds). In academic year 1980-81 it was estimated that 4 percent of the enrolled nursing students received Nursing Scholarships. Nursing Student Loans and Scholarships are awarded to schools based on statutory formula of persons enrolled on a full-time basis.

Question: What is the universe of need?

Answer: In 1980-1981, there were approximately 217,000 students enrolled in nursing educational programs. The program supported loans to over 30,000 of these individuals from both new appropriations and the revolving funds. These loans were made based on the financial need of the borrowers. The financial condition of the remaining students is not known.

Question: What effect will the loss of student aid have on already declining nursing enrollments?

Answer: The impact of reduced Federal financial aid on enrollments is really not known at this time.

Question: How will the loss of nursing student aid affect minorities?

Answer: The specific impact of the Federal reductions on minorities is not known. However, our most current data indicates that 23 percent of loans awarded by the schools from the Nursing Student Loan funds are to minorities.

Question: What other Federal support is available to nursing students, and how has this support been affected by budget reductions?

Answer: The principal source of nursing student assistance supported by this Department will be loans that will continue from the nursing student loan revolving funds that are within the institutions. In addition, graduate and undergraduate nursing students are eligible to apply for student aid programs administered by the Department of Education.

PUBLIC HEALTH SERVICE HOSPITALS AND CLINICS

Question: In the current fiscal year Congress provided $146 million for tranferring the eight Public Health Service hospitals to local or other sponsors. To what extent has the appropriation been obligated?

Answer: As of March 1, 1982, of the $146 million provided, $102 million had been obligated and $18 million had been committed for obligation. The remaining $26 million is available for mandatory reserve items such as severance pay, lump sum leave, and permanent change of station which includes the cost of shipment of household goods, transportation, and relocation of Commissioned Officers.

Of the $64.3 million specifically designated for closure and transfer of the hospitals in Seattle, Staten Island, Baltimore, and Boston, all has been obligated.

Question: How much of this money do the new local sponsors of these facilities still have in the bank and earning interest?

Answer: The funds in their entirety have been transferred to the facilities and informal conversation with the facilities indicates that all of the funds are currently on deposit in escrow accounts while each organization ascertains how to allocate the funds between construction and operating costs.

The appropriation language mandated transfer of the funds for general purposes and therefore the Department has not established specific prior approval requirements and there is no available mechanism for monitoring how the funds are expended.

The appropriation requested for these facilities was based on the minimum requirements. Therefore, in order to provide maximum flexibility for the successor organizations, the Federal Government put no requirements on how the funds were to be expended.

Question: To what extent have Public Health Service (PHS) employees of the hospitals left the Federal Service to take jobs with these non-Federal facilities?

Answer: Of 2,794 Public Health Service hospital and clinic employees who were separated from their Federal positions, 1,833 were provided some form of temporary or permanent employment with the successor organizations. The remaining 961 did not find jobs with successor organizations.

Question: What arrangements have been made for the treatment of leprosy patients who formerly received care at PHS facilities other than Carville, Louisiana?

Answer: The Public Health Service was providing specialized care to approximately 1,000 patients with Hansen's Disease in eight cities in addition to the National Hansen's Disease Center at Carville. Following closure of the PHS Hospital and Clinic System, contractual arrangements were made to meet the provisions of section 320 of the Public Health Service Act and to assure continuity of care. These arrangements include a contract with the former PHS facilities at Boston, New York, and Seattle; contracts with the Los Angeles County Health Department, the University Hospital of the University of California at San Diego, the Public Health Trust/Jackson Memorial Hospital in Miami, Mary's Self Help Hospital in San Francisco, and a small clinic operated jointly with the Louisiana State Health Department at New Orleans.

BUREAU OF COMMUNITY HEALTH SERVICES - PROGRAM SUPPORT

Question: To what extent did States request assistance during Fiscal 1982 in converting to the MCH Block Grant?

Answer: We have received a significant number of requests from the States for programmatic consultation and technical assistance during the transition to the MCH Block Grant. In fact, it is as a result of these ongoing contacts with the States that we are confident that the transition to the MCH Block Grant is proceeding smoothly. Requests have been directed to both Regional and Central office staff and inquirers have relied heavily on telephone inquiries. Additionally, requests for program assistance came from States speaking through the association of Maternal and Child Health and Crippled Children's Directors. These requests were responded to by developing guidance at the request of the Association which was made available to the States and discussed at a series of meetings between the Association, with State officials and Federal staff.

Question: Based on this experience, will the resources you will have available in 1983 be sufficient?

Answer: The resources that would be available to us would not permit us to maintain the current levels of consultation and technical assistance; however, we believe that we would have resources to provide meaningful assistance to the States.

HEALTH SERVICES ADMINISTRATION PROGRAM MANAGEMENT

Question: How will the reduced level of positions for program management affect the Health Services Administration programs?

Answer: The Health Services Administration budget requests 134 program management positions, a reduction of 63 positions in 1983. Most of this reduction, approximately 45 positions, is associated with the proposed legislation for the Primary Care Block Grant and is contingent upon that legislation being passed. The remaining position reductions are associated with the elimination of the Bureau of Medical Services.

Question: Assuming that your legislative proposals are accepted, is your request sufficient to properly manage the Agency?

Answer: The request of 134 program management positions for 1983 represents the number of positions required to administer Health Services Administration programs assuming enactment of the proposed Primary Care Block Grant legislation.

Question: How many people have been affected by Reduction in Force thus far?

Answer: Through the first quarter of fiscal year 1982, the reduction-in-force procedure has resulted in 2,815 separations and 90 down grades. Of the 2,815 individuals separated, 2,794 were associated with the closing of the PHS hospitals and clinics. These figures are for headquarters and field activities and exclude the regional offices.

Question: Are you proposing further reductions in 1982?

Answer: If the proposed reprogramming of funds to cover a portion of the 1982 pay costs for the Health Services Administration is approved by the Congress and the present Continuing Resolution is extended, we do not anticipate further reductions in fiscal year 1982.

UPDATING MEDICALLY UNDERSERVED AREAS DESIGNATIONS

Question: What is the Department doing about changing the definition of a medically underserved area for the purposes of the CHC program?

Answer: The Department is not changing the definition of a medically underserved area. Rather, we are updating the list using the most current data available. While variables used to designate MUAs have not changed, the weights associated with two of the variables have been modified. Infant mortality has been changed to reflect a decrease in the national rate and the physician to population ratio has been changed to be the same as the standard used for Health Manpower Shortage Area designations.

Question: To what degree have you examined whether any centers currently funded under the program are serving areas which can no longer be considered as underserved?

Answer: About 1,500 areas were identified as potentially losing their MUA status, based on the most current data. The number of grantees phased-out as a result of dedesignation should be in the 10-20 range; perhaps 2 or 3 percent. This is in contrast to a total estimated phase out of 200 centers, mostly those exhibiting relatively low need/demand levels and/or management deficiencies.

STATE BLOCK GRANT ADMINISTRATION

Question: What percentage of a State grant award is held aside for State administration of the MCH Block Grant?

Answer: The amounts States use for administration is not known. There is no restriction in the statute on the amount a State may use. The amount must be consistent with its report of intended expenditures. The intent of the block grant is to provide States discretion in the use of granted funds.

MEDICALLY UNDERSERVED AREAS UPDATE

Question: Why is the Medically Underserved Area update being done at this time?

Answer: We are doing the MUA update at this time because we now have, for the first time since 1976, new national data on physicians and infant mortality. The need to update the designations, using the most current data, was pointed out by both the GAO and the House Survey and Investigations Staff.

Question: Did you change the procedures and/or weightings used in the Medically Underserved Area designation process?

Answer: The variables used to designate MUAs have not changed. The weights associated with two of the variables have been modified--infant mortality was changed to reflect the decrease in the national rate and the physician to population ratio was changed to be the same as the standard used for Health Manpower Shortage Area designations.

Question: Were 1980 census data used? If not, why not?

Answer: National 1980 Census data were not used because they were not available at the time. Where current information was available at the State level it has been used.

Question: What minimum percentage of patients must come from a Medically Underserved Area for a CHC grantee to be assured of Federal funding?

Answer: The Bureau of Community Health Services has not established a minimum percentage of patients who must come from medically underserved areas. To be eligible for funding each Community Health Center must include a medically underserved area in its service area. In addition, the service area must generally be contiguous to the facility and a sufficient proportion of the target population must be within the area. Additionally, continuation applications must include extensive analysis of need/demand for health care within the service area.

MATERNAL AND CHILD HEALTH BLOCK GRANT

Question: How much is available for Cooley's Anemia projects in fiscal 1982? Will the projects in New York and New England be funded?

Answer: We cannot at this time give a specific figure for Cooley's Anemia. Our intention is to provide sufficient funds to ensure that the basic functions of current projects will continue to be carried out. The New York and New England projects will be funded, assuming that their applications are technically and programmatically acceptable.

Question: How much is available in 1982 for University Affiliated Projects? How is the cutback being effected?

Answer: We expect that approximately $10.5 million will be available to fund University Affiliated Projects in fiscal year 1982. We believe that 2 or 3 projects may not receive renewed funding and the remaining projects will receive reduced funding because of the overall reduction.

Question: How much is available in 1982 for Hemophilia projects? How is the reduction being effected?

Answer: We plan to make $2.6 million available for hemophilia projects. The reduction is being effected through a reduction in administrative overhead at the projects, an emphasis on regionalization and coordination of projects, and increased cooperation with the States.

Question: What efforts will be made by Federal, State and local levels to coordinate the MCH Block Grant with other related programs such as Medicaid?

Answer: States have indicated in their block grant applications they will participate in the coordination of activities between Early Periodic Screening, Diagnosis and Treatment, Medicaid, WIC, and other Federal programs. There is a significant number of States where these programs are already well integrated and coordinated. At the Federal level efforts have been underway for a number of years to create linkages between Title V, EPSDT, Medicaid and the WIC agencies to assure that separate funding resources were utilized in a coordinated manner at the State level. The MCH program is in the process of providing technical assistance to the States under the authority of the new law in combination with other concerned Federal agencies.

Question: What is it costing States to administer the MCH Block Grant, and does this represent increased spending or savings on their part?

Answer: There is no information available at this time which indicates the cost of administering the MCH Block Grant.

Question: To what extent could the States assume responsibility for any MCH Block Grant activities now administered at the Federal level?

Answer: States are in the process of restructuring their programs and making adjustments resulting from the block grant legislation. In fact, States are currently assuming full responsibility for a number of formerly Federal categorical programs which were administered directly by the Department of Health and Human Services. Included are the Adolescent Pregnancy, SIDS and Lead Based Paint Poisoning Prevention programs. It is anticipated that with appropriate Federal consultation, States will effectively manage these programs.

Question: Has the Secretary designated, as provided by law, an identifiable Federal administrative unit with expertise in MCH to be responsible for the MCH Block Grant?

Answer: Yes, the Program Office for Maternal and Child Health in the Bureau of Community Health Services has been given the responsibility for administering the MCH Block Grant.

Question: To what degree have budget reductions adversely affected the Federal MCH office's ability to effectively administer the Block Grant?

Answer: Budget reductions have not adversely affected our ability to effectively administer the block grant. We are continuing to provide professional and technical assistance and program consultation to States and local groups. Guidance materials have been developed by the program and are made available for use by the States if they so choose. Information is disseminated on health status and the health care needs of mothers and children. We are also providing special assistance to the States to aid in transition activities such as the phasing of genetic programs into State operations.

Question: What specific reduction in services will States have to make in programs consolidated under the MCH block grant as a result of funding decreases?

Answer: No specific reductions in services are required. States will assess the nature of the maternal and child health problem within their jurisdiction and allocate available resources based on their own established priorities and the needs of their citizens. We believe that those in greatest need and at greatest health risk will be identified through State efforts and will continue to be served.

Question: To what extent will past research and training activities be continued under the MCH block grant, and what activities will receive priority funding in fiscal year 1983?

Answer: It is not possible at this time to know the extent to which past research and training activities will be continued under the MCH Block Grant in fiscal year 1983 or the activities which will receive priority funding. We are currently examining all fiscal year 1982 activities which are supported under the Consolidated Federal Programs activity. There are 399 projects involved in this activity, including research, training, hemophilia, genetics and a variety of special service and systems projects in the States. Projects will compete for funding and we know that some will receive a diminished level of funding. The Third Continuing Resolution allowed $52.13 million for this consolidated activity, a 44 percent reduction from the 1981 level.

STATE BLOCK GRANT REPORTING

Question: What reporting activities are required by law to assure State accountability for the use of MCH block grant funds?

Answer: States must submit reports of intended expenditures. In addition, states must submit annual reports on their MCH Block Grant activities.

Question: How does the Department plan to carry out these activities?

Answer: Annual reports will be made to the Secretary for assessment and, subsequently, will be transmitted to the Congress.

Question: What kinds of uniform data will be collected under the MCH Block Grant to indicate that States are meeting program goals, such as in the area of civil rights?

Answer: States will report on activities described in the Report of Intended Expenditures. In that report, goals and objectives are indicated as are populations and localities to be served. This reporting, as well as the Annual Report, will be available for use in assessing performance.

BLOCK GRANT ADMINISTRATION

Question: What has been the impact of the MCH Block Grant on the "Program of Projects" that States were previously required to fund under the Title V program?

Answer: Programs of projects seem to remain relatively intact. Only one State has indicated an intent to discontinue projects.

Question: To what degree will States increase their own funding or rely more heavily on private sector funding to make up for Federal cutbacks in the MCH program?

Answer: We believe that the MCH Block Grant will provide the States with a degree of freedom and flexibility in administration and programming which will allow them to very substantially impact on any cutback-related problems and will enable them to continue reaching high risk, high need patients. Our expectation is that planning and resource allocation will become broader based and encompass more State and local resources, including those provided by the private sector.

Question: How will the consolidation of MCH programs into a Block Grant and the subsequent funding reduction affect State efforts to provide adequate prenatal care to pregnant women?

Answer: Health professionals, certainly those in State Health Departments and Maternal and Child Health Offices, are aware of the critical importance of prenatal care for both mother and child. In addition to the health advantages they are well aware of the cost effectiveness of prenatal care. Our expectation is that it will remain a top priority activity and that high risk/high need patients will continue to be served.

MATERNAL AND CHILD HEALTH BLOCK GRANT ALLOCATIONS

Question: How are MCH Block Grant funds allocated to States?

Answer: Currently, each State receives its share of fiscal year 1982 available funds in proportion to its share of fiscal year 1981 allotments. We have not yet determined the SWIC formula, but it will be equitable and comparable to the MCH formula.

Question: To what extent has the Department begun to examine alternative formulas for the allotment of funds to States as required by law?

Answer: A study group made up of Bureau of Community Health Services staff, officials of State and National organizations, and representatives from a consulting firm with extensive knowledge of MCH statistics are working on the development of alternative formulae. A deadline of March 25 has been set for submission of a draft report to the Public Health Service.

Question: Describe Department efforts to examine alternative formulas for the allotment of MCH block grant funds to States.

Answer: A study group made up of Community Health Services staff, officials of State and National organizations, and representatives from a consulting firm with extensive knowledge of MCH statistics are working on the development of alternative formulae. A deadline of March 25 has been set for submission of a draft report to the Public Health Service. The Department will review the factors and impact prior to recommending an alternative formula. The law requires that a report and recommendations on a revised formula be submitted to Congress by June 30, 1982.

ASSISTANCE TO STATES UNDER BLOCK GRANTS

Question: Do you plan to provide technical assistance in primary care organization, development, and operation once the Block is in place? In what way? To what extent?

Answer: For States electing the Block Grant, we shall provide technical assistance upon request. We expect the greatest demand for assistance will be in developing management information systems.

Question: What provisions are being made for the management of operational health centers in States that do not assume responsibility for the Primary Care Block Grant?

Answer: In States that do not assume responsibility for the Block, the basic Bureau of Community Health Services management approaches will continue in relationship to project grant activities. These include the Bureau Common Reporting Requirements, funding criteria, allocation systems and Federal monitoring, assessment and assistance. States will be encouraged to participate as their resources, interest, and capacity allow.

PRIMARY CARE BLOCK GRANT

Question: What activities have been initiated to facilitate transfer of the Primary Care program to the States?

Answer: All Governors and State Health Officers received letters asking for comments on the need for and efficiency of the operational CHCs in their States. The comments received in response to these letters will be incorporated into the grant review process. Medical societies also have been invited to comment upon community health centers activities in their States.

All States that express an intent to operate the block grant in fiscal year 1983 have the opportunity to participate in the review of fiscal year 1982 continuation applications.

Regional Staff have provided the States with basic information about the CHC programs --legislation, management systems, available resources, and technical assistance-- and about the individual CHC projects in each State.

Cooperative agreements have been signed with West Virginia, Virginia and Kentucky and are in the process of being finalized with Michigan, Pennsylvania and Florida. This will lead to implementation of the block grant concept prior to fiscal year 1983.

Based on these initial experiences, model cooperative agreements have been developed for modification and use in other interested States. The cooperative agreements will allow for joint grant reviews, shared project monitoring, and shared provision of technical assistance.

Question: What are the major legislative barriers or disincentives for States to assume responsibility for the Primary Care Block Grant?

Answer: Legislative changes are needed to reduce or eliminate the matching requirement; allow block grant funds to be used for State administrative costs; relax or eliminate the maintenance of effort requirements for existing grantees; and remove the required adherence to a number of statutory requirements for block grant States.

Question: Under the proposed Block Grant, how will you assure that high-need populations receive services?

Answer: Discussions with the States indicate they are aware that acceptance of the block grant carries with it a responsibility to address the issue of allocating health resources in accord with their assessments of need. Most States are aware that ambulatory care, when made accessible, can help reduce the need for more expensive care, such as inpatient health services.

We believe that State audit programs, State legislative oversight, State citizen interest, health professional and patient/consumer group involvement will combine to assure that State Agency priority setting and targeting will be effective in identifying and reaching high-risk groups.

Question: How many States have applied for grants to administer their own CHCs under the new Primary Care Block Grant program?

Answer: We have received no applications for this grant as of this time. However, we have developed cooperative agreements with West Virginia, Virginia and Kentucky which will lead to implementation of block grant programs. These States are now ready to participate in the program and we believe that they will apply.

Question: To what extent have any States which applied to administer their own CHC programs been turned down by the Secretary and, if so, for what reasons?

Answer: No States have applied to administer their own Primary Care Block Grant programs.

Question: Will any CHCs be able to secure additional support over what they already receive from State and local sources and third-party reimbursements in the coming year in order to offset the possible reductions in Federal support?

Answer: The total operating budget of the typical CHC comes from these sources: Forty-nine percent from the CHC grant; forty percent from third-party sources such as insurance, and Medicaid; and eleven percent from other miscellaneous sources. At this time there is no way to forecast whether or not centers will be able to secure more State or local support. We hope that the flexibility accorded to State operations under the Block will allow them even more readily to allocate resources available to activities which they designate as having high priority.

Question: Has the Department instituted--or do you plan to institute--any administrative efficiencies in the Primary Care Block Grant program in order to free more money for the provision of services in CHCs?

Answer: The fundamental premise of the Department's administration of block grants is to allow States great discretion in identifying problems, designing programs, and allocating resources. Reporting and other federally imposed requirements are kept to the minimum necessary to ensure the accomplishment of National goals. By distributing aid on the basis of statutory formulae and targeting it to State governmental units, uncertainty is reduced while opportunities for efficiencies in planning and administration as well as confidential accountability are increased.

This being the case, the Department does not plan to institute any required administrative efficiencies on a National basis.

Question: What reports are required from the States in the Primary Care Block Grant program and what kinds of data are to be collected to indicate that the States are meeting the goals of the program?

Answer: Two reports are required by the statute for the Primary Health Care Block Grant. The first is an annual report of progress which contains sufficient information to: determine whether funds were expended in accordance with the provisions of the statute; secure a description of the activities undertaken under the block grant; and secure a record of the purposes for which funds were spent, the recipients of such funds, and the progress made toward achieving the purposes for which the funds were provided.

The second is in accordance with the Comptroller General's standards. Insofar as possible, each State will conduct and report on an annual audit of expenditures from payments received under the block grant.

The format and specifications of the reports are left to the individual State's discretion.

FAMILY PLANNING

Question: GAO also noted the need for HHS to strengthen the role of the Deputy Assistant Secretary for Population Affairs by clarifying the position's responsibilities and instructing component agencies to cooperate with the Deputy; and to formally define program implementation research performed under Title X. What has been your response to these recommendations?

Answer: The President's 1983 Budget proposes that family planning become part of the Primary Care Block. If this block grant legislation is enacted, there would be a lesser need to reexamine the Department's responsibility. If not enacted, of course, the Department will examine the coordination issue. GAO concurred that the need for the Deputy's coordination and evaluation roles under block grants is uncertain at this time because the form of the block grants and the Federal role will not be known until they are enacted.

In fiscal year 1972, the Office of Deputy Assistant Secretary for Population Affairs and the National Center for Family Planning Services defined program implementation research funded under Section 1004 authority as Service Delivery Improvement research. This definition was based on an analysis of congressional intent as recorded in the hearings. Program implementation research, defined as Service Delivery Improvement includes the following broad areas of activity: needs assessment; operational or action research; demonstration programs; development and testing of tools and techniques; gathering of information for planning purposes, technical assistance; and evaluative research where feasible.

The Department formally submits Five Year Plan reports to Congress in compliance with the requirements of section 1009 of Title X, Public Health Service Act. In the first Five Year Plan Report, the Secretary discussed services research, planning and evaluation, and stated that "Research focused on family planning services development should be closely associated with the process of overall program planning and with the development of evaluation systems to assess achievement of program objectives...".

Question: Have any Family Planning clinics ceased operation due to funding decreases in Title X support?

Answer: We are discontinuing support to activities which have not been targeting services to highest priority. Our expectation is that about 1,000 clinics will no longer receive support through Title X. We have instructed all family planning grantees to reassess the priority populations being served and to more aggressively collect third-party payments. Given these efforts, we would anticipate that with responsible management on the part of grantees, the impact on the highest priority populations should be limited.

Question: To what degree can State or private sector funding be encouraged to make up for Federal cutbacks in Family Planning services?

Answer: The most recent data, for 1980, indicate that States, using funds available under Titles V, XIX, XX and other State and local funds, provide approximately 33 percent of the total support for family planning services.

We are instructing grantees to more aggressively collect third party and patient payments. Greater utilization of volunteers in community education activities is also encouraged.

We cannot assess the extent to which combined efforts will impact on needs, however, we believe that high risk, high need patients will be reached.

We are providing for the record information on sources of revenue for all users of family planning services, expressed by percentages.

(The information follows:)

Sources of Revenue for Family Planning Services
Calendar Year 1980

Source	Percent
Title X	49%
Title V	2%
Title XIX	6%
Title XX	13%
Other 3rd Party Payments	1%
Patient Fees	7%
State	7%
Local	4%
Other	4%
Non-cash donations	7%
Total	100%

Question: What coordination exists among Title X and Family Planning efforts under other Federal programs including Titles V MCH, XIX Medicaid, and XX Social Services of the Social Security Act?

Answer: The Omnibus Budget Reconciliation Act of 1981 established the Maternal and Child Health and Social Service Block Grants to States. Title XIX is also a State operated program. This allows for coordination to occur at the State level which is consistent with the Administration's proposal to return control of resources to the States. With respect to Title X the State health agency is the statewide grantee in 23 States and is one of multiple grantees in 22 additional States. To facilitate additional State coordination and integration of efforts, the President's 1983 budget proposes to include Title X in the Primary Care Block Grant to States.

Question: What office has responsibility to coordinate Federal Family Planning efforts, and what efforts has it made to do so?

Answer: Coordination efforts at the Federal level are carried out by the Office of the Deputy Assistant Secretary for Population Affairs. This office was established by the authorizing legislation to provide coordination, liaison and support for the administration of the Family Planning program activities within the Department.

The Deputy Assistant Secretary's Office participates in a variety of liaison activities and coordination projects on a regular basis, and serves as the focal point for family planning information. The Deputy Assistant Secretary also collaborates with responsible program groups in the development of Department policy and regulations governing Titles X, V, XIX and XX.

Question: Has the Secretary studied States' willingness and ability to assume the administration of activities under Title X?

Answer: The Administration is convinced that States are capable of administering health programs and has proposed to include family planning in the block. We have had a number of years of experience with States as grantees conducting statewide programs under the Title X project grant authority. That experience leads us to conclude that States readily can assume responsibility for family planning administration.

Question: How feasible and cost-effective would it be to: fund Family Planning services under a formula grant, or consolidate Title X under an existing block grant such as the MCH Block Grant?

Answer: We believe that it is entirely feasible to fund Family Planning activities under a formula grant. The 1983 budget proposes to consolidate Family Planning, Primary Care, Migrant Health, and Black Lung into the Primary Care Block Grant. This proposal is a significant element of the President's New Federalism initiative which will alter the relationship between the Federal Government and State and local governments by shifting decision making and responsibilities for a variety of policy, budgetary, and regulatory matters to State and local governments. Reduction in administrative requirements and facilitated State priority setting, targeting and programming should prove very cost effective for States, who would have flexibility to organize services consistent with their preferences.

FAMILY PLANNING RESEARCH

Question: What agency currently performs the Family Planning research activities previously authorized under Title X, and how have budget reductions affected these efforts?

Answer: The National Institute of Child Health and Human Development, NICHD a part of the National Institutes of Health, currently performs family planning research as it had previously done under the Title X authority. There is an increase in the fiscal year 1983 budget for the population programs of the NICHD. Consequently, there will be no effect from budget reductions in fiscal year 1983 in the area of family planning research.

Question: Describe current Family Planning research efforts.

Answer: The Center for Population Research of the NICHD supports a wide variety of studies relevant to family planning. In the biomedical fields, it supports fundamental research in reproductive processes that may ultimately lead to new methods of fertility control and to the alleviation of infertility. It also supports applied research in the development of new and improved methods of contraception and studies to provide information on the safety of contraceptive methods and sterilization. In the behavioral sciences, it supports research on the use of contraception by men and women, their reproductive values and goals and their success in achieving them. Special efforts are being directed toward the study of social and psychological factors that are involved in both the effective and ineffective use of existing contraceptive methods.

Question: Have funding cutbacks made it difficult for the Office of Family Planning to effectively administer the Title X program?

Answer: Funding cutbacks have required that we double our management efforts in administering the Title X program. The reduced funding level is proportionate to the levels experienced by other Department programs, however, it has required a reassessment of the priority populations being served and improved management of available resources.

NATIONAL HEALTH SERVICE CORPS (NHSC) PRIVATE PRACTICE OPTION

Question: The Omnibus Reconciliation Act authorized several changes in the NHSC, particularly with regard to the Private Practice Option. Which of these new provisions are you intending to implement?

Answer: One of the most positive aspects of the new legislation with regard to the Private Practice Option (PPO) is that which enables the program to finance the travel and moving expenses of the private practitioner enroute to the site in which the service obligation will be fulfilled. We plan to implement this provision in 1982, and we feel that this provision will attract a greater number of individuals into the PPO.

NATIONAL HEALTH SERVICE CORPS PHYSICIAN SUPPLY

Question: Recent studies have documented the growing supply of physicians in the country and the diffusion of physicians to smaller, non-metropolitan communities. The Graduate Medical Education National Advisory Committee has estimated that by 1990 there will be a surplus of 70,000 physicians in the country. A 1980 Rand Corporation study found that in 1977, more than 70 percent of communities with 20,000 to 30,000 inhabitants had a full complement of five different specialties; in 1960, less than a third of these communities had all five.

How many more National Health Service Corps scholarship recipients do you expect will elect the private practice option in the future, as opposed to employment in the Corps, for the fulfillment of their service obligation?

Answer: We anticipate that 300 people in 1982 and 350 people in 1983 will elect to serve the NHSC through the acceptance of this option. During the next few years, the NHSC is planning to continue vigorous programmatic activities designed to increase participation in the PPO to the greatest extent possible.

Question: What level of expenditures do you estimate will be necessary to encourage scholarship recipients to elect the Private Practice Option rather than employment in the Corps?

Answer: At the present time, it is estimated that the NHSC will spend approximately $5,000 to $7,000 in placing an individual in the PPO. This amount includes technical assistance in terms of site identification and development as well as the recently authorized ability to pay for the travel and moving costs associated with getting the PPO provider and his family to the place where he or she will serve.

NATIONAL HEALTH SERVICE CORPS (NHSC)

Question: The Reconciliation Act of 1981 extended and amended the authorities for the NHSC field and scholarship programs. Among other things, the present law authorized such sums as necessary to continue scholarship support received in the past and to award 550 new scholarships. These amendments also require the Secretary of Health and Human Services to review the designation process for health manpower shortage areas.

How many new National Health Service Corps scholarships do you intend to award in FY 1983?

Answer: The Department proposes no new NHSC scholarship awards in FY 1983.

Question: What progress have you made in reevaluating the health manpower shortage area designation process to take into account the growing number of physicians entering practice annually?

Answer: The Health Resources Administration is in the process of preparing information for a report to Congress that is due in November 1982, which will evaluate criteria to show whether the areas now designated are really shortage areas. The evaluation will propose alternative criteria taking into account demand factors and also the likelihood that a physician would come into the area in the next two years.

The Health Resources Administration plans to review all designated areas this year with the appropriate planning agencies and professional societies. Meanwhile, the review will anticipate physicians moving into a shortage area.

Question: What are your estimates of field strength requirements for the Corps in the immediate future, given findings of the dispersion of physicians to areas previously underserved?

Answer: For FY 1982 and FY 1983, the federally salaried field strength of the NHSC is proposed to be maintained at a level of 2,115 health providers. In addition, the NHSC anticipates that 300 individuals in 1982 and 350 individuals in 1983 will enter into service through the Private Practice Option (PPO). The end of year PPO field strength will be 712 in 1982 and 835 in 1983. The objective of the NHSC is to continue to provide service in the most critically and severely underserved areas. The evidence from the recent dispersion studies would indicate that there will still be a need for assigned health providers to those areas. It appears that despite the market forces, there will continue to be areas where physicians will not choose to locate voluntarily.

Question: Do you intend to require all National Health Service Corps scholarship recipients to fulfill their service obligations through practice in a health manpower shortage area?

Answer: Yes. The policy that no scholarship obligees will be released from their service obligation will remain in effect. Some will serve as federally salaried providers; others will fulfill their obligation through the Private Practice Option.

Question: How many National Health Service Corps professionals are presently assigned to Community Health Centers?

Answer: As of the end of FY 1981, 996 NHSC health providers were serving in Community Health Centers.

Question: Has the practice of assigning Corps physicians to health centers changed because of the emphasis on the Private Practice Option?

Answer: To date, the emphasis on the PPO has not significantly changed the assignment of NHSC physicians to health centers. As a matter of fact, many of the people who have elected the PPO have done so by entering Community Health Centers as salaried employees of the centers.

NATIONAL HEALTH SERVICE CORPS LOANS

Question: Why have you recommended limiting gross obligations for direct loans made by the National Health Service Corps to $1 million?

Answer: The requested levels are sufficient to meet the most important program requirements.

Question: What is the current level of these loan obligations, and what will be the impact of the proposed limitation?

Answer: These loans involve two loan programs: 1) community loans to assist in the development of NHSC sites and 2) private practice loans to assist scholarship recipients who have served at least two years of their obligation in the NHSC and who may need assistance in converting to the Private Practice Option. At the present time, the newly authorized Private Practice Loan program has not been implemented. The specific allotments of the community site development loans total $360,000 through March 1, 1982.

In terms of the impact of the loan limitations for 1982 and 1983, the request is $500,000 for each loan program in both fiscal years and it is felt that these requested levels are sufficient to meet the most important program requirements.

Question: Shouldn't such a limitation on obligations be incorporated in the authorizing statute, rather than through the appropriations process?

Answer: Under current legislative authorities there is no specifically directed limit for these loan programs. They are identified within the total authorization level for the National Health Service Corps and the annual limitations have traditionally been applied through appropriation language.

NATIONAL HEALTH SERVICE CORPS PAY COSTS

Question: You are requesting an increase of $8 million for the Corps in fiscal year 1983. It is our understanding that this may relate to your pay costs. Please explain the increase.

Answer: Of the total NHSC increase of $8.0 million, $3.5 million is identified with the annualized costs of the October 1981 pay increase in 1983. The remaining requested increase of approximately $4.5 million is for increased costs in travel, transportation, continuing education of the health providers as well as technical assistance.

1982 PAY COSTS

Question: We are told the Agency will absorb $7,447,000 in 1982 pay costs and seeks a reprogramming of $2,384,000 for the balance, a total of $9,831,000. From where do you propose to derive the reprogrammed funds?

Answer: The pay raise shortfall of $2,384,000 is proposed for reprogramming from the following activities: Community Health Centers, $1,030,000; Primary Care Research and Demonstration, $19,000; Migrant Health, $157,000; Family Planning, $518,000 and Health Professions Loan Repayments and Cancellations, $660,000.

In order to preserve programmatic funds to the greatest extent possible, we are proposing to use one-percent evaluation set-aside funds to cover the additional pay cost requirements.

Question: How will your proposed absorption of $7.4 million affect the staffing levels you propose to achieve?

Answer: We are absorbing $7.4 million of the pay costs through administrative reductions in such items as consultant services contracts, travel, equipment, other purchases and personnel lapses. Therefore, by absorbing the pay raise through these activities, staffing levels will be preserved to the greatest extent possible.

HEALTH EDUCATION ASSISTANCE LOANS (HEAL)

Question: What is the present ceiling on Health Professions Graduate Student Loans -- and is it too high or too low? Please explain.

Answer: The Administration has requested an $80 million limit on HEAL insurance. If the $80 million limitation is not approved by the Congress, the Department would conform to the statutory limit of $200 million authorized by the Omnibus Budget Reconciliation Act of 1981.

Question: What impact on the deficit results from this ceiling -- or is the effect just indirect?

Answer: The Administration's policy is to limit the amount of federally insured loans because of the impact on interest levels and potential National debt. The HEAL program is a component aspect of this government-wide problem.

EXCEPTIONAL FINANCIAL NEED SCHOLARSHIPS

Question: We understand your new budget would, contrary to previous years, provide no scholarship assistance for medical students with exceptional financial need.

Do we assume you will no longer assist students who are in exceptional financial need -- or do you have an alternative means of support?

Answer: We have not requested funds for Exceptional Financial Need (EFN) Scholarships in 1983. However, the EFN students will continue to be eligible for HPSL funds available through the schools' revolving funds. The students also will be eligible for HEAL loans.

MIGRANT HEALTH

Question: What impact has the Migrant Health Centers program made on the health status of migrant and seasonal farmworkers in the United States?

Answer: The major health problems impacting on the health status of migrant and seasonal farmworkers are in the areas of: access to care; primary care; preventive services; hospitalization and continuity of care. The Migrant Health Center Program has responded to these problems by establishing access points in medically underserved rural areas. Specifically, the program has developed 127 projects providing primary care and preventive services to 557,000 migrant and seasonal farmworkers in 32 states. Hospitalization services have been provided to 10,000 migrants primarily for high risk maternity care. In addition, there is an established referral system linking migrant projects in order to insure continuity of care.

Question: To what degree can migrant health gains be sustained in the face of budget cutbacks?

Answer: Migrant health gains can be sustained at current levels by improved coordination of Federal, State and local resources to ensure maximum utilization of existing medical resources to serve migrant and seasonal farmworkers.

Question: Where would migrant and seasonal farmworkers go for health care in the absence of Federal migrant health services?

Answer: They would utilize existing health care resources in rural areas, specifically private physician offices, local health departments and hospital emergency rooms.

BIRTHING CENTERS

Question: It has come to the Committee's attention that the Bureau of Community Health Services has initiated a particular project whose goal is to make hospital affiliated "birthing centers" available to migrant workers, and further to increase general accessibility to certified nurse-midwives. Accordingly, the Committee would appreciate learning the status of this project, and in particular, if any evaluation mechanism has been instituted which will address the issues of quality-of-care and cost-effectiveness.

Answer: There are currently two birthing centers in operation and an additional two that will become operational during fiscal year 1982. The draft program guidelines for maternity and newborn care services under which the grants were made require an evaluation mechanism which addresses the issues of degree of safety, cost effectiveness, and acceptability of the services.

LOBBYING WITH FEDERAL FUNDS

Question: What procedure do you have in place to ensure that your grantees do not use the taxpayers' funds to conduct lobbying efforts?

Answer: We do not have a special system which is specifically designed to prevent lobbying by grantees using grant funds; however, we do have various systems in place which are designed to prevent, in general, misuse of grant funds. For example, we require annual audits of our grantees. The Inspector General performs spot checks, and, in addition, we frequently advise all grantees against the improper use of grant funds, including the use of funds for lobbying purposes.

HEALTH SERVICES ADMINISTRATION PROGRAM SUPPORT REQUIREMENTS

Question: Please provide for the record a table laying out all program support requirements for HSA and explain in some detail how you plan to use this money. Wherever possible please assign a funding figure to the activity or subactivity you propose to undertake so that the Subcommittee may better understand your plans.

Answer: The program support activities of the Health Services Administration include the Bureau of Community Health Services program support, the Bureau of Health Personnel Development and Service program support, and the Office of the Administrator program management.

Priority program support activities to be supported in 1983 for the Bureau of Community Health Services include providing technical assistance to the States in the conversion of the Migrant Health, Black Lung, and Family Planning programs into the Primary Care Block Grant and the Women, Infants, and Children and Commodity Supplemental Food programs into the Services for Women, Infants, and Children Block Grant; collecting, maintaining, and disseminating information to the States on the health status of mothers and children; and closing out categorical project grants.

Priority activities for the Bureau of Health Personnel Development and Service include developing National Health Service Corps and Private Practice Option sites; placing scholarship obligors into the National Health Service Corps and Private Practice Option sites; administering the National Health Service Corps Scholarship program, including the tracking of scholarship obligors in school, in deferment status, and in service with the Corps; providing technical assistance to National Health Service Corps and PPO sites and to schools administering the loan programs; conducting evaluations of the Private Practice Option, debt management of school loan programs, and other debt management and collection efforts for all scholarship and loan programs administered by the Bureau.

Priority activities for the Office of the Administrator include performing personnel staffing, grants management and financial management functions for the Agency; administering Civil Rights, Equal Employment Opportunity, and Freedom of Information programs for the Agency; evaluation of the National Health Service Corps Private Practice Option and HEAL program; and planning, directing and administering the activities formerly in the Bureau of Medical Services, such as the National Hansen's Disease Center, Contract Patient Care for Hansen's Disease, PHS Commissioned Officers and the Federal Employee Occuptional Health program, Payment to Hawaii, the Medical Records Center, Buildings and Facilities, and coordination of the PHS portion of the Uniformed Services University of the Health Sciences.

We are providing for the record a table which displays by activity the program support funding requirements for the Health Services Administration along with an explanation of proposed use of these funds. The requirements are contingent upon passage of the 1983 budget proposals.

[The information follows:]

1983 Program Support Funding Requirements
(dollars in thousands)

Program Support Activity	HSA Component: Bureau of Community Health Services	HSA Component: Bureau of Health Personnel Development and Service	HSA Component: Office of the Administrator	Total, Health Services
Total	$8,979	$16,764	$6,875	$32,618
Personnel Salaries and Benefits	7,288	10,786	5,740	23,814
Rent, Communications, Utilities, and Other Services	1,291	4,126	930	6,347
Printing and Reproduction, Supplies and Equipment	45	290	100	435
Travel and Transportation	275	800	105	1,180
Project Contracts	80	762	---	842

Explanation:

Of the $32.6 million requested for Health Services Administration program support activities, $23.8 million, or 73 percent, will support personnel compensation and benefits costs of 560 positions requested for these activities; $6.3 million, or 19 percent, will support costs of rent, communications, utilities, and other services; and $435,000 will fund printing and reproduction, supplies and equipment costs. Of the remaining $2.0 million, $1.2 million will be used for travel and transportation and $842,000 will be used for project contracts, both of which are required to effectively carry out the programs administered by the Health Services Administration.

PAYMENT TO HAWAII FOR TREATMENT OF HANSEN's DISEASE

Question: What will be the impact of closure of the Public Health Service hospitals on continuation of the Hansen's Disease activity in Hawaii.

Answer: The Payment to Hawaii for Treatment of Hansen's Disease is a separate budget activity in the Health Services Administration. The closure of the Public Health Service hospitals and clinics had no impact on this activity.

Question: To what extent will costs of the Hawaiian program increase in Fiscal Year (FY) 1983 over FY 1982, necessitating a larger appropriation in the new fiscal year?

Answer: The Health Services Administration's 1983 appropriation request for the Payment to Hawaii is $1,732,000, which is $158,000 less than the 1982 Continuing Resolution level. The 1983 request will provide 50 percent of the State's total program cost, as compared with 60 percent provided in 1982.

SUBCOMMITTEE RECESS

Senator RUDMAN. We thank you and your colleagues for being here today.

The subcommittee will stand in recess, subject to the call of the Chair.

[Whereupon, at 2:53 p.m., Monday, March 2, the subcommittee was recessed, to reconvene at 9:30 a.m., Tuesday, March 3.]

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 1983

TUESDAY, FEBRUARY 23, 1982

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, D.C.

The subcommittee met at 9:30 a.m. in room 1318, Everett McKinley Dirksen Senate Office Building, Hon. Mark Andrews presiding.

Present: Senators Schmitt and Andrews.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

STATEMENT OF DR. MURRAY GOLDSTEIN, ACTING DIRECTOR

ACCOMPANIED BY:
- **DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH**
- **WILLIAM MATTHEWS, BUDGET OFFICER**
- **ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. The subcommittee will come to order.

Yesterday we began our hearings on the fiscal year 1983 budget for the National Institutes of Health, and we continue those hearings this morning with testimony from Dr. Murray Goldstein, Acting Director of the National Institute of Neurological and Communicative Disorders and Stroke.

Doctor, we welcome you. Please introduce your colleagues, and then give us a brief summary of your opening statement, which will be included in the record in its entirety.

INTRODUCTION OF ASSOCIATES

Dr. GOLDSTEIN. Thank you, Senator Andrews.

On my right, Dr. Thomas Malone, Acting Director of the National Institutes of Health.

On his right, Mr. Anthony Itteilag, Deputy Assistant Secretary for Budget of the Department of Health and Human Services.

On my left, Mr. William Matthews, Budget Officer of the NINCDS, and immediately behind him Dr. Katherine Bick, the Acting Deputy Director of the Institute.

Senator Andrews, thank you for the opportunity to discuss with this subcommittee the present status of research and research training programs of the NINCDS. The Institute's written report describes in some detail the activities of the Institute. However, a few summary comments may be of assistance.

SUMMARY OF PROGRAM

I am very pleased to have been able to report on the existing opportunities available at this time which permit us to address these, the most devastating of illnesses that can afflict mankind—disorders of the brain and the nervous system, hearing, and that uniquely human ability, language and speech.

For example, the concern and the terror associated with learning that a loved one has a brain tumor, the sense of helplessness associated with becoming a paraplegic, the frustration of not being able to talk because of a stroke, and the long-range concern for the welfare of a child who is deaf. Understanding the human brain is truly a challenge worthy of our society. Disorders of this organ threaten us with the loss of the ability to perceive, to think, to remember, and to perform, the loss of ability to be a contributing member of our family and our community.

For the past three decades, this subcommittee has generously supported a national effort to understand how the brain works and to develop methods of preventing its diseases and disorders. I must admit we still do not understand how the brain works, how it perceives the environment, stores and recalls information, and coordinates every function of the body.

It will be many years before we have the answer to these important questions, but each year in an orderly, step-by-step process, important progress is being made. I can assure you of that.

We do not foresee any giant breakthroughs in the immediate future. However, we know a great deal more this year than we did last year, and next year we will know even more.

We now have methods and instruments that without physically invading the brain can observe and measure it at work, in health and disease.

These methodologies give us the opportunity to answer questions that were unapproachable just 5 years ago. And as a result of this research, we are making impressive advances against disorders of the nervous system.

Senator Andrews, the NINCDS intramural and extramural research programs have been extraordinarily productive in establishing a base for preventing and treating these disorders. The opportunities for continuing this successful national endeavor have never been more available and the promise never greater.

I trust my written statement has more adequately described these programs of the NINCDS for the subcommittee. I will be pleased to try to respond to any questions you may have about them.

Thank you, sir.

PREPARED STATEMENT

Senator ANDREWS. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. MURRAY GOLDSTEIN

Fiscal Year 1982 has been a year of continued progress against the most devastating and frightening illnesses that can threaten man--disorders of the brain and nervous system. If we lose the ability to recognize our surroundings because of defects in our sensory apparatus such as occurs in hearing loss, or if we are not able to hold a cup or to walk or to control our urinary bladder because of spinal cord or motor nerve injury, we become dependent upon others to meet the most basic needs of our activities of daily living. Of perhaps greater consequence, if we lose the ability to think, to remember, to communicate or to coordinate our activities because of brain disease, we lose our individuality as unique persons and our role in the family and society as independent, contributing human beings. The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) is the national focal point for defining through research how the brain and nervous system work, why they fail to work, how to prevent these failures, and if disorders do occur, how to minimize their effect. Fiscal Year 1983 offers us important opportunities for continuing this progress through NINCDS support of basic research and clinical investigations both in our intramural laboratories in Bethesda and nationally by means of our competitive research grant and contract programs.

Of all major systems of the body, the nervous system remains the least understood. There are as yet no meaningful models of how the brain, a unique organ about the size of a fist, can take information which is delivered to it from all parts of the body, analyze it, accept some--reject others, store it for a lifetime or use it almost instantaneously to perform a coordinated and sophisticated act. The most advanced computer we have or are even planning, is a toy in comparison to the brain. Until just recently we were unable to approach systematically an understanding of how the brain works. Neither the basic building blocks of information were available nor was the technology for the coordinated examination of cerebral structure on a molecular basis and cerebral metabolism on a cellular basis. Thirty years of focused research have now given us the insights and methods needed to approach this task. The promise for results in our lifetime were never greater; the opportunities never more available. Neurochemists working jointly with molecular neurobiologists are unlocking the functional apparatus of the nerve cell, how it works, how it stores information, how it transmits this information to other nerve cells and of most importance, through local circuitry and transmitters, how the cell modulates its own activities--cellular biofeedback. As a result of neurobiological research going on today, we are on the threshold of knowing how the nervous system functions as the master regulator and coordinator of most body functions.

Basic neuroscience research is preparing us for achieving our most important goal: prevention. Once a nerve cell dies, it cannot be reborn. This is true in the ear, the spinal cord, or in the brain. Thus, if we are to prevent the 600 known diseases of the nervous system, we must understand the process which goes astray, the biological point of diversion within that process, and the metabolic, immunological and pathological consequences of that diversion, which we call pathogenesis. In 1983, we will give even greater attention to identifying the vulnerable points in pathogenesis at which therapy can intervene to prevent the death or malfunction of the nerve cell. An example of this research is the phenomenon of the neurotropic viruses. Certain viruses (e.g., rabies; western equine encephalitis; and perhaps unknown viruses which may cause multiple sclerosis) seek out the nervous system in which to live and multiply. As a consequence, they selectively destroy the nervous system. Why this viral affinity for the nervous system? Can we block that affinity? We think so. In our intramural and grant supported laboratories we are developing man-made, harmless viruses that will trigger the nervous system to develop immunity to pathological neurotropic viruses. This immune reaction, something like that produced by a vaccine, has the potential to prevent infection of the nervous system. This becomes particularly important when we recognize that in addition to the well-known, acute infections of the nervous system like rabies or encephalitis, we also have long-incubating chronic infections of the nervous system which may be the underlying cause of multiple sclerosis, brain tumors, amyotrophic lateral sclerosis and dementias such as Alzheimer's disease. Thus rejection of the neurotropic virus by the nervous system would make it immune from invasion and the development of disease.

Another aspect of this same problem of pathogenesis and prevention is the non-antigenic virus-like particle. The nervous system recognizes a foreign particle such as a virus because it is a foreign protein; having recognized it, the immunological response combats the invader and attempts to overcome it. However, we have preliminary evidence that certain neurotropic virus-like material, instead of destroying the nerve cell, may actually become part of the cell's own genetic material. It can live as part of the cell undetected for decades but when triggered by another infection or environmental toxin, it becomes active and causes disease. Certain brain tumors and some dementias might very well be due to this non-antigenic latent virus. We are attempting to identify these particles in animals and to learn of their properties and role in disease.

However, useful methods of prevention are still not available for most neurological and communicative disorders. Thus, in the interim, attention to the development of improved methods of diagnosis, treatment and the restitution of function must continue. Let me repeat, once a nerve cell dies it cannot be reborn or replaced. However, in traumatic injury to the brain and spinal cord, very often only the communicating fibers of the nerve cell are damaged. The injured cell fiber dies back towards the cell body and a new fiber grows, attempting to make functional connection with its previous target--a muscle, another nerve cell, or a visceral organ. This regrowth process is called neuronal regeneration. This process occurs relatively easily in the peripheral nervous system as in arm or leg injuries, but it does not occur in higher animals whose central nervous systems are injured. Accidents are the fourth leading cause of death in the U.S. and traumatic injury to the brain and spinal cord is a leading reason for these deaths. However, when death does not occur, lifelong disability such as paraplegia is often the tragic consequence. NINCDS has designated neuronal regeneration as a research area for focused attention since only through research can methods be developed so persons with spinal cord or brain injury can become able-bodied again. Research progress has been and continues to be encouraging. We now know the injured central nervous system axon of higher animals can regenerate; we do not yet know why the regenerating neuronal fiber won't grow across the area of injury and make functionally useful connections. However, one by one, the biological variables controlling this process are being identified. It would be premature to guess when successful functional regeneration of the CNS will be a reality, but every known method for accelerating research and achieving accomplishment is being pursued.

Stroke continues to be the number one neurological problem in the U.S. Despite remarkable advances made in the control of hypertension and in acute stroke therapy, the number of strokes which do not kill but instead destroy areas of the brain continues to be high. Thus, the stroke victim in the 1980's usually does not die but rather survives with life-long disabilities. In any population, this is unacceptable but in an aging population because of an increased occurrence of stroke, it is socially disastrous. NINCDS supported stroke clinical research centers have been developed as national focal points for identifying risk factors whose control can prevent stroke, for developing methods to protect the brain cells during the acute stroke episode so that there can be a maximal return of function, and for improving surgical and pharmacological therapies. We must remember that stroke is several different disorders, each due to a different cause, each affecting a specific area of the brain which reacts in its own unique way to ischemia, and each requiring specific therapy. There has been major progress against stroke mortality over the past two decades and neurological research being supported at this time offers promise of even more success for prevention of brain damage and the return of threatened body function.

Neuropharmacology, the study of chemicals that act as agonists (mimickers) or antagonists of neurotransmitters, has given scientists new insight into many movement disorders (parkinsonism; Tourette syndrome) and developmental and genetic disorders (autism; Huntington's disease). These are rare diseases and pharmaceuticals in these areas are often referred to as "orphan drugs." In cooperation with the pharmaceutical industry, the NINCDS has developed and is actively engaged in a functional protocol for jointly developing and evaluating needed new orphan drugs in the area of epilepsy. In 1983 we will explore the adaptation of this productive relationship in epilepsy to other tragically incapacitating neurological and communicative disorders.

The communicative and sensory disorders including hearing loss, language impairment such as aphasia, and disorders of smell and taste are an important aspect of the NINCDS research program. These are probably the most poorly appreciated of the serious disturbances of mankind. Society can easily recognize a blind person; but unless there is direct contact, it rarely recognizes a deaf or hearing impaired person. For example, hearing loss is often the cause of poor performance and is confused with mental disorders, a too often occurrence in the elderly; also, dyslexia--the inability to read properly--is too often confused with mental retardation in children and young adults. These organic disorders of the nervous system's communicative and sensory apparatus are poorly understood and have not received the attention they deserve. To remedy this situation, the NINCDS is organizing specific programs to address the research issues in this field. Two intramural laboratories have been established, one for basic research and one for clinical research. By means of research grants, communicative disorder and sensory disorder research centers are being funded to provide for multi-disciplinary teams to address these research issues. These newly organized intramural laboratories and extramural research centers also will serve as national research training resources to recruit and prepare the needed basic and clinical research personnel. It is too early to report on the success of this targeted effort, but the Institute looks forward to being able to do so in the near future.

Time does not permit me to describe the specific effort and progress being made in the many other disease areas of NINCDS responsibility. Developmental disorders such as spina bifida and cerebral palsy, Reye's syndrome, autism, epilepsy, the dementias such as Alzheimer's disease, the demyelinating disorders such as multiple sclerosis, the atrophic disorders such as amyotrophic lateral sclerosis, and brain tumors are but a few. There are no easy ways or short cuts to foster a better understanding of the brain and its disorders, but the intramural and extramural research programs of the NINCDS are moving ahead steadily and soundly towards the achievement of this goal through research. The ultimate resource for continued progress in neurological and communicative research is skilled research personnel. The Institute's research training and research career development programs see to it that a core cadre of basic and clinical investigators is available to incorporate the most recent advances into the research of the future. As a result of these Institute research and research training programs, 1983 promises again to be a year of steady progress and achievement against the neurological and communicative disorders.

In conclusion, the budget request for the National Institute of Neurological and Communicative Disorders and Stroke for 1983 is $274,505,000. I am pleased to have the privilege of sharing this information with you and will try to answer any questions you may have about these matters.

BIOGRAPHICAL SKETCH

NAME: Murray Goldstein, D.O., M.P.H.

POSITION: Acting Director, NINCDS

BIRTHPLACE & DATE: New York, New York; October 13, 1925

EDUCATION:
B.A., New York University, 1947
D.O., Des Moines Still College of Osteopathic Medicine, 1950
M.P.H., University of California, School of Public Health, 1959

EXPERIENCE:
Acting Director, NINCDS, 1981-present
Deputy Director, NINCDS, 1978-1981
Medical Officer, Commissioned Corps, PHS (Assistant Surgeon General), 1953-present
Director, Stroke and Trauma Program, NINCDS, 1976-1978
Director, Extramural Programs, NINCDS, 1961-1976
Visiting Scientist, Mayo Clinic and Graduate School, Rochester, Minnesota, 1967-1968
Chief, Special Projects Branch, NINCDS, 1960-1961

Asst Chief, Research Grants Review Branch, DRG, 1959-1960
Actg Chief, Section on Virus Diseases of the CNS, Bureau of Acute Communicable Disease, Calif. State Dept of Public Health, 1958
Director, Epidemiology and Biometry Training Grant Program, DRG, 1956-1958
Asst Chief, Grants and Training Branch, NHI, 1953-1958

ASSOCIATION MEMBERSHIPS:

American Academy of Neurology
American Association for the Advancement of Science
American Heart Association, Council on Stroke
American Neurological Association
American Osteopathic Association
Association for Research in Nervous and Mental Disease
Society for Neuroscience
The American Parkinson Disease Association, Medical Advisory Board
Eisenhower Institute for Stroke Research
United Cerebral Palsy Research & Educational Foundation Board of Directors
Consultant, World Health Organization Program on Neurosciences
World Federation of Neurology
International Brain Research Organization
Commission on Alternative Health Care, U.S. Olympic Council on Sports Medicine

SPECIAL AWARDS, CITATIONS, OR PUBLICATIONS:

Beta Alpha Epsilon; Biology National Honor Society, N.Y.U.
Psi Chi; Psychology National Honor Society, NYU
Sigmi Alpha; Osteopathic Scholarship National Honor Society; College of Osteopathic Medicine
Delta Omega; Public Health National Honor Society; Univ of California
Doctor of Science (Hon); Kirksville College of Osteopathic Medicine
Certificate of Merit; American Neurological Association
Silver Star; Purple Heart, U.S. Army
Meritorious Service Medal; Public Health Service
Associate Editor, Stroke, A Journal of Cerebral Circulation, American Heart Association
Editorial Board, Osteopathic Annals
Editorial Board, International Journal of Neurology
Editorial Board, The Journal of Neuroepidemiology
Author of over 20 scientific papers and monographs

ORPHAN DRUGS

Senator ANDREWS. Doctor, in your written statement you mention orphan drugs. We have had some constituent support for the Orphan Drug Act which was introduced last September in the House. The bill provides flexibility, as I understand it, in the drug approval process for these drugs for rare diseases and provides incentives to pharmaceutical companies for producing these drugs.

What effect would the Orphan Drug Act have on the work you are doing in your Institute, Doctor? Have you had a chance to review this act?

Dr. GOLDSTEIN. Yes; I know the bill very well. The Department and the National Institutes of Health are presently examining the bill in order to determine the specifics of its impact upon our programs. And if I may, sir, may I respond to that question for the record.

Senator ANDREWS. I'd appreciate it if you would.

[The information follows:]

IMPACT OF THE ORPHAN DRUG ACT

The Assistant Secretary for Health of the Department of Health and Human Services, in his testimony on March 8, 1982, before the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce said:

"I think that you and I are in agreement that the time has come for a comprehensive effort involving coordination of governmentwide activities as well as expanded liaison with groups outside government. In this regard, the Secretary today announced his intention to establish an orphan drugs and products board, which I will chair. Like the committee envisioned in H.R. 5238, it will consist of representatives from appropriate DHHS agencies and other Government departments and agencies. We plan to invite individuals from the Veterans' Administration, the Department of Defense, and others to participate. We believe that the board will have a broader scope and more responsibility than the committee proposed in H.R. 5238. I hope, therefore, that you will agree that our board initiative—which requires no new legislation—is worthy of your support.

"Because our efforts will be broader in this respect, our priorities will have to be carefully established. 'Orphan drug' means many things to many people, and there are almost as many terms to describe an orphan drug or product as there are definitions. This variety of viewpoints has tended to blur the issues and create conflicting and, at times, unattainable expectations. We will need to offer assistance to all who genuinely need our help, but we must be careful to establish realistic objectives for the program. The board will provide a forum for discussion and resolution on this point.

"The purpose of the board would be to set policy in this area by facilitating the research, development, and approval of designated orphan drugs and products. The board will work actively with the PMA Commission on Drugs for Rare Diseases in identifying and assigning priorities to products that need development or other assistance to secure marketing approval. It will identify needs and foster action within the Government to expedite the development and approval of orphan products."

The Department board will identify and foster action within the Government to expedite the development and approval of orphan products. The board will consist of senior DHHS officials from the Food and Drug Administration, Centers for Disease Control, National Institutes of Health, Alcohol, Drug Abuse, and Mental Health Administration, Health Care Financing Administration, and others as appropriate. Representatives from other Government departments, such as the Department of Defense, Veterans' Administration, and the Department of Commerce, as appropriate to carry out the mission of the board, will serve as liaison members. The designated board members will be knowledgeable agency officials having decisionmaking authority and substantive knowledge of their representative agency's programs pertaining to orphan products.

I believe this board will be of great importance to furthering the orphan drug and other products development responsibilities of the NINCDS. We look forward to active participation.

Senator ANDREWS. One other question on that. Was this bill put together with your people's help or was it a totally independent one coming out of the blue at you?

Dr. GOLDSTEIN. The answer is a little bit of both, sir. A survey of the several Institutes at NIH which are involved in the evaluation and development of orphan drugs was conducted by the staff of the congressional committee.

As a result of the information from that survey, parts of the bill were developed. And so indirectly the NIH was involved. We contributed factual information. We did not ourselves participate either formally or informally in the development of the specific language of the bill.

NIH PERSONNEL

Senator ANDREWS. Before I continue on questioning you specifically, Dr. Goldstein, I'd like to ask Dr. Malone a question about the impact of bumping the NIH personnel and the Public Health Service officers that were affected by the transfer of the Federal hospitals to non-Federal status. I was concerned about breaking up a well-trained group in your clinical center. I am aware the group has acquired some additional personnel, and so far so good.

But my question is: How well did NIH fare overall in this matter and how many trained NIH staff members were bumped by other personnel which may have had the seniority but lacked the specific training to take over their jobs? Obviously, they are therapists, obviously they are Government employees. No one knows the seniority system better than I who had 18 years of seniority and had to start over again in the Congress. But when you displace people and replace them with others, sometimes you destroy good teams that have been established over the years. What was the result of all this?

Dr. MALONE. Senator Andrews, I can fully appreciate the thrust of your question. The NIH overall has fared extremely well. Indeed, in consideration of the thousands of individuals who have been RIF'd or RIS'd from their positions, we have lost only six individuals, and these were in the areas of nutrition and in the social science areas mandated by the so-called bumping procedure.

On the other hand, we have absorbed some 400 individuals from other parts of the Department who otherwise might have lost their jobs. We do not foresee any further impact on the situation in the near future.

Senator ANDREWS. What about the impact of the reduction in strength on staff morale and productivity?

Dr. MALONE. I think that there might have initially been some concern. There was perhaps some negative impact on the morale of the staff, but I think that has been completely reversed. There is no indication that we are now in a situation where we would expect any further reduction in our staff.

Senator ANDREWS. As I understand, the reports we got were that you handled it quite well once you recognized the type of problem you had and the people with seniority were accommodated, and the research teams that you had put together were not split up either.

Dr. MALONE. Yes; that is absolutely correct.

FISCAL YEAR 1983 BUDGET

Senator ANDREWS. Again, back to the Institute at hand, the budget proposes to cap indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent, and to maintain training allowances slightly below the fiscal 1982 level. What will these policies do to your research and training efforts, Dr. Goldstein?

Dr. GOLDSTEIN. There are two separate issues there, sir. First is the indirect cost issue.

As you know, Senator, a grant is a conditional gift to an institution to assist it in accomplishing what it itself has proposed to do and wishes to carry out. The issue has been raised both in regard to indirect costs and to actual direct cost about what proportion of the costs of that research should be shared by the Federal Government with the grantee institution. It is in that philosophy that both the indirect costs and direct cost reductions have been thought through.

I am certain that we are going to find that the grantee institutions will find it difficult to absorb cuts in both areas, and therefore may have to be even more selective than they are at the present time in determining which research areas the institutions will be able to proceed through the grant program.

Senator ANDREWS. What will it do to the ability of grant recipients to produce good science and good research?

Dr. GOLDSTEIN. It will clearly slow them down some. In other words, the scope of work will have to be decreased and prolonged over a period of time.

IMPACT OF THE 1982 CONTINUING RESOLUTION

Senator ANDREWS. What has been the impact of the 1982 continuing resolution which imposed the lower of the House and Senate figures, if I recall, or a 4-percent reduction beyond that?

Dr. GOLDSTEIN. On the grant programs, sir?

Senator ANDREWS. That is right.

Dr. GOLDSTEIN. What it has meant is that each one of the projects has had to have been negotiated with both the principal investigator and grantee institutions in an attempt to learn how we can, in an orderly way, decrease the scope of the activity and yet maintain its principal research thrust. And so it has increased the one-to-one negotiations with these investigators and institutions in an attempt to accomplish our overall purposes within budgetary constraints.

FISCAL YEAR 1983 CUTBACK

Senator ANDREWS. Will this budget require cutbacks or revisions in your previous plan for 1983?

Dr. GOLDSTEIN. Yes, sir.

Senator ANDREWS. In significant areas? Will you cut out all new areas of research or will you conduct your research in all of these various areas but at a reduced rate?

Dr. GOLDSTEIN. Both, sir. In the areas of the highest priority, we will continue our thrust, but at a slower rate. In other areas of activity we will have to postpone implementation until a future year.

Senator ANDREWS. Do you have the flexibility so that the cuts will fall largely on your contract research, or will it be applied on in-house research as well?

Dr. GOLDSTEIN. Our cuts will apply across the board, sir, in-house, contract, and extramural grants.

RESEARCH CENTERS

Senator ANDREWS. How much are you spending on research centers in fiscal 1982 and how much will you spend in fiscal 1983?

Dr. GOLDSTEIN. In fiscal 1982, assuming the continuing resolution continues at that level for the entire year, we will spend approximately $21.8 million for our research center program.

In fiscal year 1983, that program amount is proposed to be at $22.8 million. This is at a level necessary to meet our commitments. There will be no additional centers initiated.

Senator ANDREWS. What economies can be achieved in this area without impairing essential research and activities—you know, this waste, fraud, and abuse syndrome that we hear so much about.

Dr. GOLDSTEIN. I see, sir. Well, let me try to address it this way.

In our spinal cord injury area, we have five multidisciplinary research teams at work in different parts of the country, some supported as centers and others as program projects. We honestly did feel that five units were a critical mass which permitted the effective interaction needed nationally.

What we will be required to do, I believe, is to attempt to choose among the five active programs and discontinue one in order to maintain the critical mass within each of those remaining. That is the kind of judgments we will face both in 1982 and in 1983 in order to maintain the thrust of the research effort, continue its momentum, but decrease the amount of activity involved specifically.

Senator ANDREWS. Could you put in the record, Doctor, where these centers are and how much each receives so we have a sense of it?

Dr. GOLDSTEIN. The spinal cord programs or all the centers, sir?

Senator ANDREWS. All the centers.

Dr. GOLDSTEIN. Yes, sir.

[The statement follows:]

NINCDS RESEARCH CENTERS

Principal Investigator Institution Location Project Title	FY 1981 Award
Snow, James B. Jr. University of Pennsylvania Philadelphia, Pennsylvania Clinical Smell and Taste Research Center	$396,307
Glaser, Gilbert H. Yale University New Haven, Connecticut Neurological Research Center/Epilepsy	451,432
Prince, David A. Stanford University Stanford, California Epilepsy Research Program	421,957
Gumnit, Robert J. University of Minnesota Minneapolis, Minnesota Minnesota Comprehensive Epilepsy Program	708,587
Ward, Arthur A. Jr. University of Washington Seattle, Washington Center for Clinical Research in Epilepsy	1,387,832
Bourke, Robert S. Albany Medical College Albany, New York Brain and Spinal Cord Trauma	208,904
Matz, Gregory J. University of Chicago Chicago, Illinois Sensory Disease Clinical Research Center	574,974
Ward, Paul H. University of California at Los Angeles Los Angeles, California Communicative Disorders Clinical Research Center	714,097
Berlin, Charles I. Louisiana State University Medical Center New Orleans New Orleans, Louisiana Peripheral and Central Auditory Mechanisms	494,437
Hirsh, Ira J. Central Institute for the Deaf Saint Louis, Missouri Auditory Communication and Its Disorders	835,788

Principal Investigator Institution Location Project Title	FY 1981 Award
Duvall, Arndt J. III University of Minnesota Minneapolis, Minnesota Mechanisms of Auditory and Vestibular Dysfunction	$608,653
Paparella, Michael M. University of Minnesota Minneapolis, Minnesota Otitis Media Pathogenesis (Clinical Research Center)	458,908
Koprowski, Hilary Wistar Institute of Anatomy and Biology Philadelphia, Pennsylvania Etiology and Pathogenesis of Multiple Sclerosis	959,872
Silberberg, Donald H. University of Pennsylvania Philadelphia, Pennsylvania Etiology and Pathogenesis of Multiple Sclerosis	836,032
Bornstein, Murray B. Yeshiva University New York, New York Pathogenesis and Treatment of Multiple Sclerosis	879,815
Oldstone, Michael B. Scripps Clinic and Research Foundation La Jolla, California Pathogenesis of MS and ALS	793,054
Asbury, Arthur K. University of Pennsylvania Philadelphia, Pennsylvania Studies of Neuromuscular Diseases	723,438
Weiner, Norman University of Colorado Health Sciences Center Denver, Colorado Basal Ganglia Disorders and Neurotransmitter Function	656,926
Katzman, Robert Yeshiva University New York, New York Biogenic Amines and Neurological Disorders	300,683
Yahr, Melvin D. Mount Sinai School of Medicine New York, New York Clinical Research Center--Parkinson's & Allied Diseases	501,435

Principal Investigator Institution Location Project Title	FY 1981 Award
Abbs, James H. University of Wisconsin Madison Madison, Wisconsin Speech Movement Research with an X-Ray Microbeam	$690,669
Ransohoff, Joseph New York University New York, New York Clinical Research Center for Acute Spinal Cord Injuries	566,889
Plum, Fred Cornell University Medical Center New York, New York Research Center in Cerebrovascular Disease	1,221,107
Scheinberg, Peritz University of Miami Miami, Florida Research Center for Cerebral Vascular Disease	800,383
Davis, James N. Duke University Durham, North Carolina Duke-V.A. Center for Cerebrovascular Research	557,733
Toole, James F. Wake Forest University Winston-Salem, North Carolina Cerebrovascular Research Center	354,934
Whisnant, Jack P. Mayo Foundation Rochester, Minnesota Mayo Cerebrovascular Clinical Research Center	639,014
Raichle, Marcus E. Washington University Saint Louis, Missouri An Interdisciplinary Stroke Program	595,895
Halsey, James H. Jr. University of Alabama in Birmingham Birmingham, Alabama Cerebrovascular Disease Research Center	924,832
Meyer, John S. Baylor College of Medicine Houston, Texas Cerebrovascular Research Center	324,644

Principal Investigator Institution Location Project Title	FY 1981 Award
Taveras, Juan M. Massachusetts General Hospital Boston, Massachusetts An Interdepartmental Stroke Program	$717,792
Reivich, Martin University of Pennsylvania Philadelphia, Pennsylvania Cerebral Blood Flow and Metabolism in Stroke and Shock	1,051,321
Price, Thomas R. University of Maryland at Baltimore Baltimore, Maryland Clinical Stroke Research Center	712,730
TOTAL	22,171,074

PROGRAM MANAGEMENT

Senator ANDREWS. In light of these current restraints of the budget and the need to put adequate funds into research, you talked about savings that you can achieve in direct operations and program management in fiscal 1983.

What are your most important administrative concerns?

It is kind of a blue-sky question.

And what are your least important concerns?

Dr. GOLDSTEIN. The most important concerns we have are, as I explained in my opening statement, that the neurological and communicative sciences are truly an exploding area of research. The methodologies and techniques that we have been longing for for 25 years are now with us. We can examine the human brain without entering it; we can watch it work.

In order to accomplish this, extraordinarily expensive technology is required. What we will have had to do is cut back on the rate of obtaining that technology in our direct operations. This is a very important concern.

Second, we will have to be extraordinarily lean in the recruitment and maintenance of our high-class staff. As an example, we have never really had the ability to understand the central processing of hearing—how does noise that we hear get interpreted by the brain so that you can understand what I'm saying. We are in the process of developing such a laboratory in our intramural program as a national focal point, both for research and for training other people who will enter the university system in the future.

Obviously in these frugal direct operation years we will have to cut back on the speed of moving ahead with the implementation of our plan.

TECHNOLOGICAL DEVELOPMENT

Senator ANDREWS. Doctor, when you talk about new technology, new devices, new methods, you are really the center for this type of research in the United States if not in the Western World.

Let's say a given pharmaceutical firm or a given health-care firm comes up with a new development that they think may work. Do they give this to you to work with? Do you buy these machines, commission them made, or do you have a partnership relationship—and I have checked this out with the clerk and he doesn't know the answer either, and I learned long ago never ask a question in this business if you don't know the answer. John Rooney would turn over in his grave.

But I frankly don't know the answer, and I am interested in whether you have a working understanding with the industry so that when they come up with some new technology, do they let you have it so you can do work with it and in effect give them the reports back to inform them whether or not they really have something?

Dr. GOLDSTEIN. Actually both goes on, sir. A large proportion of these technologies are actually developed in the university environment in collaboration with industrial development.

As an example, one of the newest methodologies available to us is nuclear magnetic resonance, NMR. This technique is a new world of instrumentation, which is moving ahead very rapidly. It is being developed jointly by the industrial and academic world. A small, really a relatively small proportion of the funds for its development is coming through the NIH or any government agency.

Now, when that technology evolves, two things occur.

In the case of NMR it has such important clinical significance that there will probably be no need for future Federal investment in its development and evaluation. Very much like the CAT scanner or CT scanner, this development will be centered in the industrial environment. When we need such an instrument, we will have to buy it, and we are making such plans.

On the other hand, there are technologies that are developed jointly by Government with industrial involvement. When that instrumentation becomes available we then usually share in its evaluation and development with industry at usually no cost or relatively little cost.

REDUCTION OF NEW RESEARCH GRANTS

Senator ANDREWS. Your budget, Doctor, proposes to reduce new research grants from 221 to 171. Can you explain the rationale for this reduction?

Dr. GOLDSTEIN. Sir, the issues that we have are twofold.

One, the average cost per grant continues to increase. This is not only a function of inflation—inflation is clearly a function—but it is also a function of the kind of technology and very highly skilled personnel that are required. So the average cost per grant is going up.

Second, of course, is trying to live within our budget and to make very difficult decisions so that we target the most important research. When one does the addition and adds it up, those are the resources we will have available to accomplish our purposes.

Senator ANDREWS. What research areas in particular will receive reductions in funding and with what effect?

Dr. GOLDSTEIN. Probably two areas, sir.

One, we will have to cut back on our plans for clinical trials, cut back in the sense that the clinical evaluation of the new drugs and surgical procedures will have to be postponed to a future year. The second area will be in the development of new applied information. There we will attempt to work more closely with industry and with the private sector in an attempt to move ahead with those, despite the decreasing impact of Federal funding.

ORPHAN DRUG ACT

Senator ANDREWS. Now, the Orphan Drug Act you mentioned in your original statement and I questioned you about in my initial question——

Dr. GOLDSTEIN. Yes.

Senator ANDREWS [continuing]. That would address itself to part of this, but does it carry an authorization for separate funding for this type of thing?

Dr. GOLDSTEIN. No, sir; the Orphan Drug Act does not carry any financial authorization as part of it. This is the act recently introduced by Mr. Waxman.

Senator ANDREWS. Yes, but I understand it does include some tax credits.

Dr. GOLDSTEIN. For industry, sir.

Senator ANDREWS. But would those tax credits be used for you to do that type of thing?

Dr. GOLDSTEIN. Not directly, sir.

Senator ANDREWS. So actually the work that you are having to cut back in this field is actually what the Orphan Drug Act is in effect addressing?

Dr. GOLDSTEIN. Yes, sir.

BUDGET INCREASE

Senator ANDREWS. While you are cutting back on new research, you are at the same time increasing funding for overhead and intramural research. What accounts for this inconsistency?

Dr. GOLDSTEIN. Two factors, sir. First, a very, very large proportion of that increase is mandatory salary increases.

Mr. Matthews, would you say that is about 75 percent of the increase?

Mr. MATTHEWS. It is all of the increase.

Dr. GOLDSTEIN. All of the increase for direct operations and program management are due to mandatory salary increases.

SUBMITTED QUESTIONS

Senator ANDREWS. Thank you very much, Doctor. I have some other questions that I'd like to ask for the record, and if you can provide the answers at the same time that you return the corrected hearing transcript we will receive it then.

Dr. GOLDSTEIN. Thank you very much.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

BUDGET CUTS

Question: Have budget cuts had a substantial effect on your Institute's priorities?

Answer: The NINCDS conviction that our three areas of equal priority are support of extramural research grants, research training and intramural research activities has not changed. Budget cuts have constrained progress in each but have not materially altered these priorities.

REDUCTION IN NEW GRANTS

Question: Your budget request proposes to reduce new research grants from 221 to 171 -- a cutback of 50. What research areas in particular will receive reductions in funding?

Answer: The reduction referred to involves only new competing grants. It does not include competing renewals of ongoing projects. Competing renewals are being retained at essentially the same level as in FY 1982. In making fewer new competing awards, we shall reduce awards across most disorder categories rather than concentrating reductions in one or a few selected categories.

Question: With what effect?

Answer: The effect of this reduction will be to stretch out the time required and defer progress in basic and clinical research.

Question: While you are cutting back on new research, you are, at the same time, increasing funding for overhead and intramural research. What accounts for this inconsistency?

Answer: The increases in overhead and intramural research consist primarily of mandatory increases of $2,781,000 to cover within-grade salary increases, payments for centrally furnished services, telecommunications costs increases, increased payments to the Federal Employees Compensation Fund, and increased costs of routine services and supplies. These increases do not represent program expansion. In addition, $457,000 is included to replace obsolete research equipment and to complete the equipping of the Communicative Disorders Clinical Research Branch which is being organized during FY 1982.

RESEARCH CENTERS

Question: How much are you spending on research centers in Fiscal 1982 — and how much will you spend in Fiscal 1983?

Answer: The 1982 budget for 32 specialized research centers is $21,852,000. The 1983 budget provides $22,836,000 for these centers.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: We are carefully reviewing all research activities proposed within each center. As a result of interactive consultations with each center director, we are proposing delay of initiation of those research activities for which such a delay would not significantly affect the overall research thrust of the center. We are also encouraging center directors to explore private sector sources for partial funding for specific activities.

CLINICAL RESEARCH

Question: We note you plan to increase your clinical research program by $2.6 million (from $89.2 million to $91.8 million) in fiscal 1983. Please bring us up to date on the progress you are making in clinical research.

Answer: The dollar increase of $2.6 million maintains critical elements of our clinical research program at the current level.

NINCDS supported much of the research leading to L-dopa, the first effective drug for Parkinson's disease. Recent work has led to other drugs and new formulations of L-dopa for Parkinson's disease and other movement disorders.

In Alzheimer's disease, the most common form of dementia, NINCDS grantees have recently shown that cells in one specific area of the brain die, demonstrating that this disease is more than a nonspecific consequence of aging.

The new imaging technique of positron emission transverse tomography (PETT) has identified abnormal metabolic function in the brains of patients with stroke, in the specific area which causes a seizure in epilepsy, and in patients with Huntington's disease as well as in brain tumors.

Recent clinical studies show that interventions designed to reduce swelling of nervous tissue and improve blood flow increase survival in patients with severe brain and spinal cord injury, and may lead to better restoration of long term function.

The development of better methods of treatment of otitis media by NINCDS grantees has dramatically reduced the risk of permanent hearing damage. Research and advanced development of cochlear prostheses have the potential for partial restoration of sound cues for the profoundly deaf adult. Prescription fitting of improved hearing aids also should soon be possible.

The decrease in age adjusted mortality rates for stroke over the past 30 years is attributed to better understanding of risk factors such as transient ischemic attacks (little strokes) and better control of hypertension. Newly developed diagnostic tools by NINCDS grantees are providing the clinician with better knowledge of the kind of stroke a patient has, thus aiding in more rational management to limit damage and promote better recovery.

From 1974-1981 NINCDS supported research has played a major role in the introduction of four new drugs for control of epileptic seizures. Approximately 400,000 Americans whose seizures were not well controlled previously have benefited.

NINCDS supported research has led to better understanding of the disorders of immune function seen in myasthenia gravis and multiple sclerosis. This will provide a rational basis for development of new therapies for these diseases.

The understanding of the basic genetic defect in diseases such as Tay-Sachs, Gaucher's and Fabry's has led to replacement of the missing enzymes to reverse the buildup of the stored compounds which cause the symptoms. The strategies developed in these research efforts should be applicable to other neurogenetic diseases.

CLINICAL TRIALS

Question: To what extent does your funding request provide for clinical trials?

Answer: The budget requested would allow continuation of selected trials of novel anticonvulsant drugs for epileptic seizures for which currently available therapies are inadequate. Studies to test therapies for hemorrhagic strokes would be initiated on a small scale. Dependent on the scientific opportunities, small trials of alterations of the immune state in multiple sclerosis may be undertaken. Clinical trials to evaluate promising treatments for early use in brain and spinal cord injury are proposed. The effect of drugs on movement disorders such as Parkinson's disease will be studied.

HUNTINGTON'S DISEASE

Question: What was the purpose of your field trip to Venezuela in connection with Research on Huntington's disease?

Answer: The Lake Maracaibo area of Venezuela presents a unique field research opportunity since it contains a major focal point for Huntington's disease resulting from the isolation of the population and a high degree of intermarriage. In accordance with a recommendation of the Huntington's Disease Commission report, the NINCDS initiated a field study in FY 1981 to Venezuela in order to compile patient pedigrees, and obtain samples of blood and skin from selected members of several large families who evidenced an unusually high incidence of Huntington's disease.

Question: What was the cost?

Answer: The cost to the NINCDS was $143,000 in FY 1981 and the FY 1982 estimate is $97,700. In addition, the Venezuelan government provided salary and logistic support estimated at $15,000 in FY 1981 and $20,000 in FY 1982.

Question: What were the results?

Answer: Detailed family histories were obtained from 125 persons. Skin, and/or blood samples were taken from 112 of these subjects, and delivered to tissue culture facilities in the United States. This material will permit validation of new diagnostic tests for Huntington's disease currently under development by NINCDS grantees.

Preliminary analysis of the pedigrees has identified one individual in the remote fishing village of Lagunetas who may have inherited the Huntington's disease gene from both parents. If confirmed, this circumstance, not known to have occurred previously, may permit precise localization of the Huntington's disease gene on a specific chromosome.

TRAINING INCREASE

Question: Your Institute seems to be going in the opposite direction from NIH on the subject of research training. Overall in 1983 NIH plans to reduce the number of trainees by 8 percent, from the 1982 level of 9,709 to a total of 8,915. On the other hand you want to increase the number of trainees over the 1982 level to bring it back up to the 1981 level. Please explain your plans in this regard and tell us why you differ from NIH in general on the subject of research training.

Answer: The proposed increase in the number of trainees for the NINCDS for FY 1983 is based on trends in research training over the past several years. When pre-1973 training authority was converted to the National Research Service Award, the NINCDS training programs were reduced at a rate disproportionate to the NIH as a whole. Also, the NINCDS research training budgets have not kept pace with other Institutes in the years since the new authority was passed. During this period, the training of clinical investigators has fallen below a critical level. Hence, the proposed increase in the number of trainees for FY 1983 is an attempt to begin to rectify past differences and to alleviate shortages in critical research areas.

INFLATION

Question: When forecasting funding levels necessary for FY 1983, what figure has been used to factor in inflation?

Answer: The Department guidelines assumed an 8 percent inflation factor in developing the 1983 budget requests.

Question: Has last year's factor of 9.5 percent proved to be realistic?

Answer: The increase in average costs for grants is variable depending on the type of grant, competing or non-competing status and also depends on the mechanism, e.g., research projects, centers, or research career programs. Considering these variables, the 9.5 percent factor appears to be a realistic projection for 1982.

Question: To what degree were additional cuts made in FY 1982 in such areas as travel, consultant services, and personnel compensation?

Answer: The Institute has effectively managed its travel budget and saved approximately $100,000 from the original estimate for 1982. Consultant services have been reduced approximately $120,000. Personnel compensation will be extensively reduced as a result of continuation of the hiring freeze. These combined savings will be used to absorb the FY 1982 pay raise costs of approximately $1.5 million.

Question: Did you operate under a hiring freeze throughout 1981?

Answer: The NINCDS has operated under a hiring freeze throughout 1981 which restricted us to hiring within the Department of Health and Human Services only. Appointments from outside the Department have been approved as exceptions to the freeze in only a few occasions where we were able to demonstrate a critical need and after an extensive search for qualified individuals had been made within the Department.

POSITRON EMISSION TRANSVERSE TOMOGRAPHY (PETT)

Question: Is the PETT Program fully funded and operational at this point or do you anticipate significant expenditures in this area in the future?

Answer: The NINCDS intramural and extramural Positron Emission Tomography (PETT) Program is fully funded and is operational at this time. Major extramural research efforts are being carried out at 11 institutions throughout the country with collaborative efforts at others. It is anticipated that continued support will be required for research using PETT in the future, although major capital equipment purchases have already been made in most of the involved research centers.

Question: To what extent are we already making use of this new technology?

Answer: Although the various extramural research centers utilizing PETT technology are in differing stages of their development, considerable information is already being developed concerning both normal brain metabolic activity as well as that of the diseased brain. With PETT, we can determine changes in metabolic activity by the increase or decrease in consumption of glucose, oxygen or other labelled substances by the brain tissue. Investigators are currently mapping those areas in the normal brain which show increased activity secondary to motor, visual or mental activity. A comprehensive baseline of normal brain function is being developed which is then being compared to the abnormalities created by disease processes.

PETT is being used in patients with stroke to determine more precisely those areas of the brain involved in the stroke and to measure quantitative changes in energy consumption and blood flow in these areas in order to correlate pathology with the potential for recovery. PETT will provide useful information on proposed new treatments.

PETT is currently being used to identify the metabolically active and inactive areas of the brain in patients with brain tumors. As drugs for brain tumors are positron labelled and thus can be identified in the PETT scanner, their concentration within the tumor bed can actually be measured. Patients with epileptic seizures are studied in order to localize the areas of dysfunction more precisely. The alterations in metabolic activity, before, during and after seizure activity will help in the design of better therapeutic regimens. PETT technology can also be applied to a wide variety of other diseases including alterations secondary to head trauma, Alzheimer's disease and other dementias and other brain disorders.

During the past year, over 100 PETT scans were performed by the NINCDS intramural research program. Focusing on patients with brain tumors, epilepsy, and Alzheimer's disease, this research has amply demonstrated the great importance of the PETT technique for the regional localization of the pathogenesis of several neurologic disorders.

EPILEPSY

Question: What has come from your Drug Development Program with respect to new drugs to treat epilepsy?

Answer: Since 1974, four drugs have become available to the public to treat epilepsy through development sponsored by the NINCDS.

Many more drugs are in early stages of evaluation and development for epilepsy. Over 6,000 compounds have been screened and about 3,000 found to have activity in preventing seizures. Of these, 110 have appeared promising enough to be subjected to the most advanced animal tests and a number of new and different compounds are approaching the clinical stages of development. Three have been entered into clinical trials. Besides testing these drugs, the program has sponsored trials in epileptic patients of new drugs obtained from outside the screening portion of the program.

Question: What drug products have been made available to the public as a result of this development program?

Answer: Four drug products have been made available to the public because of clinical trials supported by this development program. These are carbamazepine (Tegretol), clonazepam (Clonopin), valproic acid (Depakene), and clorazepate (Tranxene).

STROKE

Question: The incidence of stroke in the U.S. for 1977 was 137 cases per 100,000 population and is dropping. The rate of stroke incidence for 1986 is expected to be 118 per 100,000. Are statistics indicating a continued decline in the incidence of stroke still considered valid?

Answer: The statistics indicating a decline in the incidence of stroke are based on the National Survey of Stroke. As the methodology used in the Survey has been validated, the projection of a continued decline in the incidence of stroke is considered sound.

Question: Please provide us with figures on the rates for 1980 through 1983.

Answer: The estimated incidence rates of stroke per 100,000 for 1980-1983 based on the National Survey of Stroke are:

1980 - 130.2
1981 - 128.1
1982 - 126.0
1983 - 123.9

Question: NINCDS stated last year that if stroke research programs continue to make progress as anticipated, there would be a diminishing need for funds in the future in the areas of stroke prevention and acute therapy. Can you demonstrate a reduction in the cost of research as a result of gains made in the prevention of stroke?

Answer: It is not possible to demonstrate currently, nor even to project for the near future, a reduction in research costs as a direct result of gains made in the prevention of stroke. This is true because clinical investigators must consider the problems posed by the significant numbers of patients who still get strokes. Stroke is still a leading cause of death and permanent disability. Thus, attention is being directed toward improved methods of prevention, research into the care of patients who have had a stroke, and in whom recovery can be anticipated, as well as improved interventions in those with residual disabilities. While important progress has been achieved in preventing some types of stroke through the control of hypertension and reduction of other stroke risk factors, research in the less easily addressed areas of stroke prevention and treatment must be maintained. Improved methods of early diagnosis, therapy to limit, or even reverse the extent of damage of a stroke-in-evolution and restoration of function in patients with completed stroke are all of high priority. In the long term, we would anticipate that success in these areas will lead to decreased stroke research costs.

SPINAL CORD RESEARCH

Question: In 1981 there were reports in the news media about a promising new drug treatment for preventing total or partial paralysis resulting from crippling spinal cord damage. Apparently the drug has been used experimentally in cats and was able to significantly reduce paralysis associated with spinal cord trauma. What can you tell us about this new drug TRH?

Answer: Thyrotropin-releasing hormone (TRH) is a tripeptide that has a number of physiologic effects in addition to its function in regulating the release of the hormone thyrotropin from the pituitary gland. Among these effects is its ability to act as a partial block to the body's own pain killing substance (opioids). The opioids have been causally associated with markedly reduced blood pressure following profound injury. This generalized hypotension may result in diminished blood flow and irreversible damage to the injured spinal cord. The TRH, in blocking the action of the opioids, may serve to help sustain blood flow to the spinal cord; thereby reducing the effect of the injury and improving the return of function following recovery from the initial injury.

Question: Did you play an active role in the development of the drug?

Answer: TRH is a naturally-derived substance that has been studied extensively for a number of years, primarily with respect to its effects on the endocrine systems of the body. Its non-endocrine functions have received increasing scrutiny by NINCDS supported investigators in recent years. These studies led to the experimental testing of TRH in cats with recently sustained spinal injuries by investigators associated with the Walter Reed Army Institute of Research and the Uniformed Services University of the Health Sciences.

Question: Can the drug be produced in large quantity through synthesis or will such procedures as the recombinant DNA molecule technique have application in its production?

Answer: Thyrotropin-releasing hormone probably can be isolated, synthesized or derived through relatively conventional manufacturing techniques.

Question: Has the Food and Drug Administration granted approval for the use of this drug in clinical trials?

Answer: The Food and Drug Administration has not granted approval for the use of this drug in clinical trials. Additional animal testing is required before human trials can be conducted.

OTHER DISEASES

Question: What progress are you making against the following diseases: multiple sclerosis; amyotrophic lateral sclerosis; Huntington's disease; autism; and Reye's syndrome?

Answer: The following are short descriptions of progress on several of the neurological disorders.

Multiple sclerosis--Progress is being made in investigating the cause, improving the accuracy of diagnosis, monitoring the clinical activity, and assessing the efficacy of new treatments in multiple sclerosis (MS). New approaches in molecular biology and immunology are being used in studies of putative etiological agents for demyelinating disease, such as measles virus in humans and a self-replicating, non-nucleic acid containing pathogen in animal models of MS. Defects in immune regulation have been identified in patients with MS. Such abnormalities are being investigated in identical twins to determine etiological factors and to develop effective therapies. Several clinical trials of agents which modulate immune response in human patients are underway.

Amyotrophic lateral sclerosis (ALS)--New hypotheses regarding etiology have been developed and are being tested. Abnormalities of lipids in the brains of some patients with ALS have been identified. Highly preliminary data suggest a relative decrease in serum testosterone levels in male and an absolute decrease in female patients with ALS. A dog model which has clinical and pathological features similar to the human disease is being studied. The abnormalities seen in these dogs, particularly those relating to transport of various chemicals along the length of the nerve fiber, are being investigated. Metabolic studies of calcium metabolism of patients and controls in high-incidence foci in Guam (where levels of certain minerals in soil and water are markedly deviant from normal) have been done and the significance of the data is being analyzed.

Huntington's disease--Study of the possible abnormal proteins produced in the body by the gene responsible for the development of Huntington's disease (HD) may provide a reliable early diagnostic test for the disease. Research is being conducted to identify the abnormal gene in non-neural tissue to facilitate presymptomatic diagnosis. Animal models of Huntington's disease are being developed to permit more rapid and efficient testing of drugs to prevent or ameliorate the abnormal muscle movements and mental deterioration.

Autism--Approximately one-third of children with childhood autism are essentially without speech and language abilities and remain untrainable and dependent for their entire lives. Using new training techniques, some children who were previously unreachable have acquired some communicative skills; they can understand both single spoken words and signs and also can use some signs to communicate their needs to others. New approaches to language training focus on the speech rhythm and sentence structure difficulties experienced by autistic children once they have acquired a vocabulary of several words. The NINCDS also conducts and supports a number of basic research studies which are relevant to the fundamental processes which may be the basis of autism, such as research on the maturation of neurotransmitter pathways in the development of motor control and arousal behavior.

Reye's syndrome--Increased public and professional awareness of Reye's syndrome has resulted from wide-spread publication of the report from the NIH Consensus Development Conference on the Diagnosis and Treatment of Reye's Syndrome. Such public and professional education leads to earlier identification and treatment of Reye's syndrome and should improve survival rates and prevent sequelae. In addition, NINCDS sponsored scientists are investigating brain circulation, ammonia metabolism, and cell lipid metabolism, as well as conducting virologic and immunologic studies in an animal model. Two possible treatment regimens are also being evaluated.

SPECIAL REVIEW

Question: Title V of the Health Programs Extension Act of 1980 directed HHS to enter into a contract with the Institute of Medicine to review neurological and regeneration research, to identify promising areas, and to develop a five-year plan for neurological research. This review was due to be completed by December 1981. What is the status of the review?

Answer: The statutory authority for this review was made contingent upon funds being provided in advance by an appropriation act. Funds for this purpose were not provided in the appropriation for NINCDS. Nevertheless, the Institute is in substantial compliance with this provision.

In 1979 the Institute completed a comprehensive review of the state-of-the-art of the neurological and communicative sciences including research on spinal injury and regeneration. The report of this review, entitled the National Research Strategy for Neurological and Communicative Disorders, detailed research opportunities and provided a five-year blueprint for pursuing these opportunities including budget, training and personnel requirements. A copy of this multi-volume assessment was provided to the Appropriations Committee.

In addition, in 1979, the Institute sponsored a status report specifically on Central Nervous System Trauma Research. This report, edited by Dr. Guy Odom, Professor of Neurological Surgery at Duke University, provides a detailed technical assessment of current research on spinal cord injury and regeneration.

These reports, taken together, provide the assessment and planning contemplated by P.L. 96-138.

Question: Have you gotten any preliminary use from it?

Answer: The NINCDS utilizes these planning documents in formulating its program plans and budget requests. They are also used as measures to assess actual progress.

PROJECT WITH INDUSTRY

Question: Last year you mentioned a joint effort with industry for the development of agents to diminish clots in cerebral vessels. This effort is an attempt to cope with the large aspect of the nation's stroke problem which is not associated with high blood pressure. How are you progressing with this project?

Answer: Investigators conducting stroke research in the United States are participating with industry in the evaluation of drugs which have been shown to possess potential for preventing the formation of blood clots in cerebral vessels. Specifically a protocol has been developed and is being implemented in which patients will be accrued into the study over the next several years. Significant follow-up results may be expected in approximately five years.

Question: If such drugs were developed, what patients would become your target population for such medication?

Answer: The target population would be patients who have experienced indications of impending stroke such as transient ischemic attacks or so called "little strokes." They are patients who are at high risk of having further transient ischemic attacks or a more devastating completed stroke.

Question: Would drugs of this type be used on a long-term basis following a diagnosis that a patient was at high risk of cerebral infarction?

Answer: Although the exact answer will not be known until we have had more experience, it could be expected that long-term preventive management could be instituted following the diagnosis of a patient at high risk of cerebral infarction in order to reduce the chance of additional cerebrovascular accidents. Full demonstration of safety and effectiveness must await additional information which will become available over a period of time on possible drug side effects and long-term toxicity.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

STATEMENT OF DR. RICHARD M. KRAUSE, DIRECTOR

ACCOMPANIED BY:

DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. BERNARD TALBOT, DEPUTY DIRECTOR
DR. KENNETH SELL, SCIENTIFIC DIRECTOR
CHARLES E. LEASURE, JR., EXECUTIVE OFFICER
YVONNE H. DU BUY, BUDGET OFFICER
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. Dr. Krause, our next witness, is Director of the National Institute of Allergy and Infectious Diseases. Dr. Krause has appeared before the subcommittee many, many times, and on behalf of the subcommittee I want to welcome you again. I also want to thank you for sending along the copy of your book, "The Restless Tide." Our clerk is as impressed with it as I am and in fact I am going to send it on to my daughter who happens to be in medical school at the present time. She graduated in biochemistry so it's right up her alley. It's written so even an individual who graduated in agronomy, as I did, can understand it.

Dr. KRAUSE. Thank you.

Senator ANDREWS. I appreciate your sharing it with me.

If you can introduce your colleagues and give us a brief summary of your opening statement, we can begin.

INTRODUCTION OF ASSOCIATES

Dr. KRAUSE. Yes, sir. First of all, to my left is Dr. Talbot, the Deputy Director.

And I would like to take this opportunity, Senator, if I may, to be sure that you meet Dr. Sell, who is the Scientific Director. Dr. Sell is responsible for all intramural activities, including the clinical activities, of our Institute. And it just so happens he was born in Cass County. He is a graduate of the University of North Dakota. I thought you might want to know that he was awarded the Sioux Distinguished Alumnus Award of the University of North Dakota. For those in the audience who do not know how to spell Sioux, that's S-i-o-u-x.

Senator ANDREWS. And, Doctor, might I point out that there was an

Easterner that came West who was advised by a group of newspaper editors that if he'd go out and mess up a few Indians, they'd make him President of the United States. His name was George Armstrong Custer. The Sioux didn't cooperate [laughter], and that's one of the first lessons of how inaccurate the advice the Eastern political writers give is. [Laughter.]

The county from where your colleague comes from—Cass County, N. Dak.—happens to be my home county. I am a recipient of the Sioux award, too, and they almost choked when they gave it to me because I graduated from the other university, a land-grant institution.

But we've got a host of good friends up there and both of my daughters have gone to the University of North Dakota, so you've got a good man in your department. If only we could have more North Dakota natives—you know, 40 below eliminates the riff-raff [laughter], so we have very strong stock out there. The breeding, you know, comes along quite nicely—survival of the fittest. You've got a very competent man in your shop.

BIOLOGICAL REVOLUTION

Dr. KRAUSE. During the course of my remarks, sir, I'll point out that we have some of our work going on out in your part of the country.

May I begin this way: Medicine—since you have read my remarks in my book "The Restless Tide"—has been seized with a revolutionary fever—the biological revolution, it's called. And medicine, as we knew it, will never be the same again. At the heart of this new revolution is a process called recombinant DNA technology. We are promised new vaccines, new miracle drugs and other cures for diseases that still elude us. Some predict that the influence on agriculture, in fact, will be even greater than the influence on medicine. There will be perhaps hardier crops, which are more resistant to insects and molds than those we now have. "The genetics gold rush," the British magazine, The Economist, has labeled this whole matter on the cover of a recent issue. On its cover is a cornucopia of plenty emerging from recombinant DNA technology.

Let me in these few minutes describe how this biological revolution is extending the horizons of this Institute for the prevention and treatment of disease.

Three brief points, sir.

First, the influence of the revolution on the accelerated development of new vaccines.

Second, the influence of this revolution on research at the NIAID Rocky Mountain Laboratories in the Bitterroot Valley of Montana; research that is concerned with a disease in sheep called scrapie, a model for chronic disability diseases in man.

And third, ways in which medicine and agriculture must work hand in hand if we are to improve the health for all in this crowded world. Disease and hunger are the two major epidemic plagues on the globe; and if we are wise enough and sensible enough, the biological revolution just might see us through these troubled times.

ACCELERATED DEVELOPMENT OF NEW VACCINES

Now, first a comment on vaccines.

We have a program for the accelerated development of new vaccines, fired by this biological revolution.

One example that I would give you is that of hepatitis B, a disease in this country which still afflicts at least 150,000 people; many develop serious complications, including death. Epidemiologic evidence suggests this is an infection that may lead to liver cancer.

The vaccine we now have is composed of hepatitis B particles. These are isolated from the blood of infected individuals. We have not yet grown this virus in the test tube, so we must harvest it from infected individuals. Through research done in this Institute and many of the others at the NIH, and then through the work conducted by Merck, this vaccine has now been licensed and is now available. But the supply will be limited because we cannot grow the virus and it will be expensive because of the manufacturing process.

But can we manufacture it by processes that employ the techniques of the biological revolution?

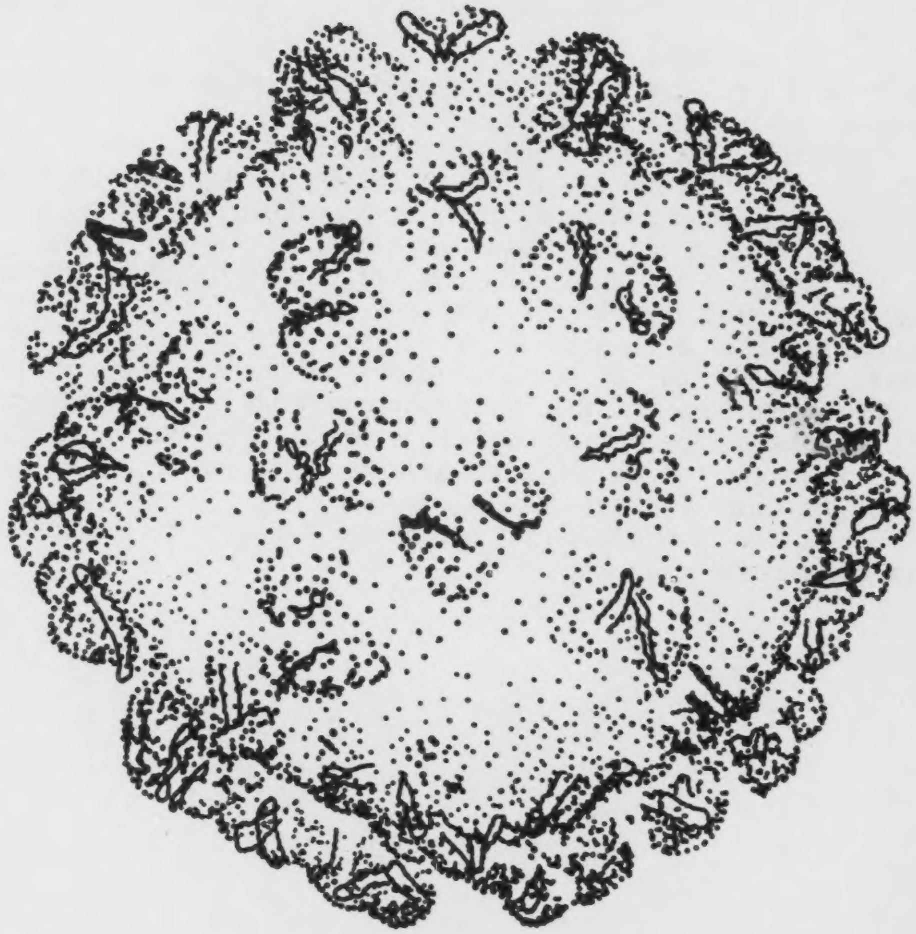

FIGURE 1.—Computerized view of a single hepatitis B virus particle.

Let's examine a computerized view of a single hepatitis virus particle—figure 1. You will notice on the surface there are a series of wart-like projections. And those wart-like projections are what actually stimulate the immunity when one receives the vaccine.

Now, we can't prepare this whole virus particle in the test tube, but what we can do is produce these wart-like projections that stimulate immunity with recombinant DNA technology.

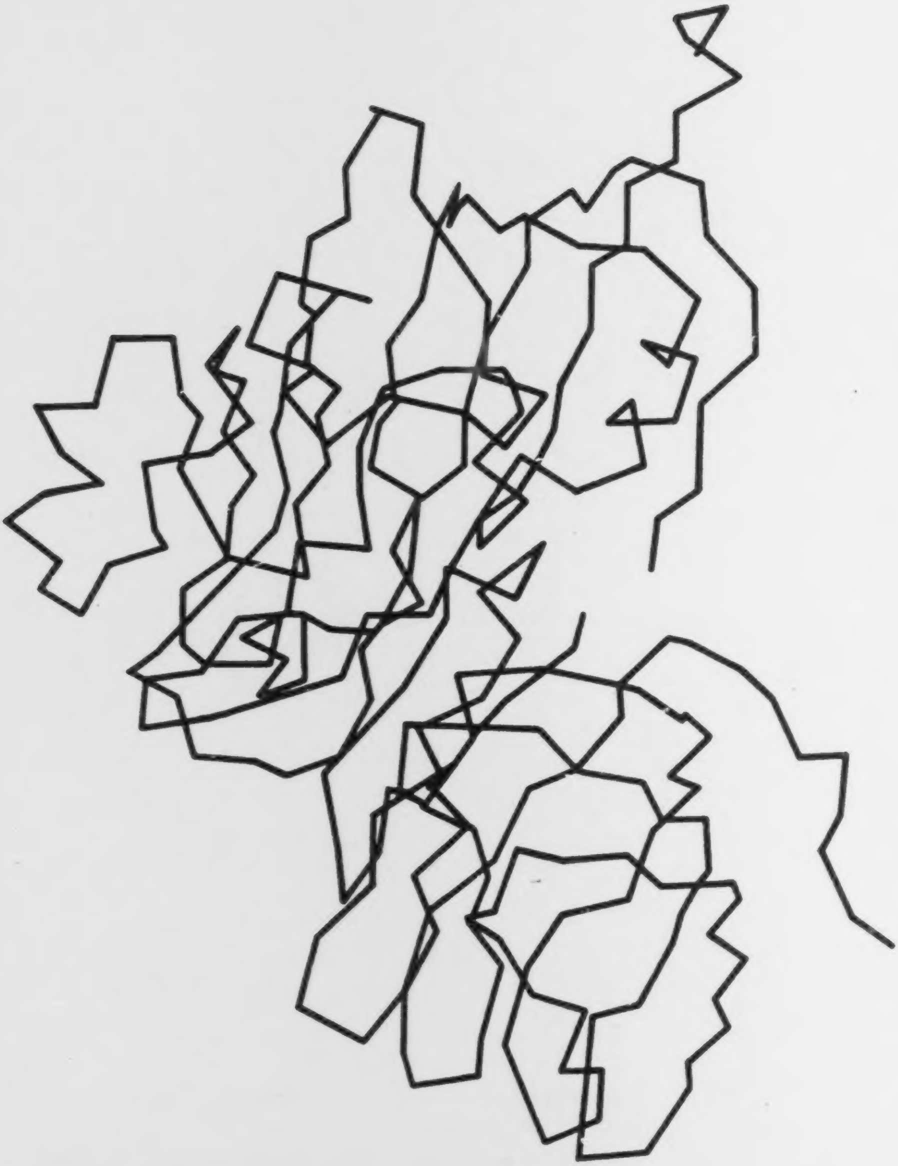

FIGURE 2.—Computerized version of the chemical nature of immunity-stimulating property of hepatitis B virus particle.

Figure 2 shows the complex computerized version of the chemical nature of one of these wart-like projections that stimulate immunity. These are now being produced by recombinant DNA technology. So it may be possible to prepare the vaccine by a chemical process.

In figure 2, you will note a small portion colored orange; you will recall the whole virus particle I showed you earlier was sprinkled over the surface with orange patches. This orange portion is the business end of this huge molecule. It is this and this alone, this small portion, that stimulates the immunity. Can we in fact synthesize this small bit itself, only that small portion of the total virus particle?

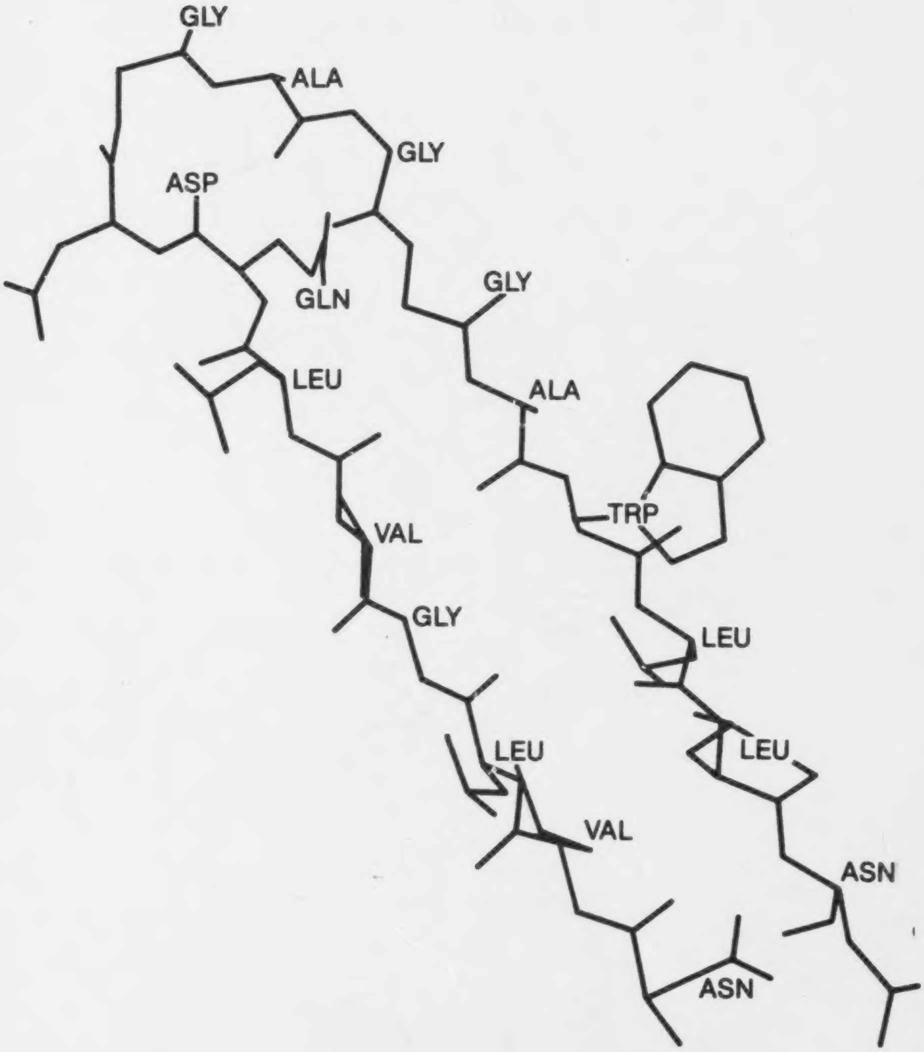

FIGURE 3.—Chemical structure of synthesized hepatitis B virus.

Well, in fact this has been done. The chemical structure is shown in figure 3. It is not a large compound, only 20 amino acids long. It has been produced in the test tube. Scientists at the NIAID have tested it in chimpanzees and it induced immunity.

So what I have tried to give in this brief glimpse of the future of hepatitis B vaccine is how all this new modern biology is being used to circumvent the fact that we have not been able to grow this virus. But in fact it has been possible to synthesize the single smallest portion of it that stimulates immunity. These developments will lead to the second and third generations of hepatitis vaccines.

ROCKY MOUNTAIN LABORATORIES

Now, I must tell you about a portion of this Institute that is up there where the temperatures are also 40 below.

The Rocky Mountain Laboratories are in the Bitterroot Valley of Montana and have a history that goes back to the first part of this century. But most important, for 30 years, scientists there have pursued the elusive nature of the disease in sheep called scrapie. If you know sheep farmers, then you perhaps have heard of this disease. It is a degenerative disease of their nervous system due to peculiar infectious particles. The nature of these particles is still uncertain, although there have been recent reports in the New York Times on their possible nature. Yet work which has been done in our Rocky Mountain labs has provided some idea about the nature of these very strange infectious particles and what their characteristics are that cause this disease in sheep.

The reason that we are concerned about the importance of this problem is that in some way this may very well be a model for some strange chronic diseases which already have been mentioned at these hearings, such as presenile dementia, as well as other chronic diseases.

I have overstepped my leave here, so I will not go on with the third point I wish to make on the important relationship between agriculture and medicine.

I would only say this, that most of the people of the world are poor and sick, and yet American grain is supplying the bulk of these people with food. Where will they get the money to pay for that except through U.S. aid programs? But is there not a better way?

I have said that the world is gripped by the despair of disease and hunger, and surely that despair will continue to swell on our shores and will not recede until we realize that health for all means wealth for all. Wealth follows health; the matter is not the other way around.

I believe our research program on tropical diseases such as malaria, which afflict 500 million people in this world, will improve the health of the world's poor, and with that their wealth.

Here, again, the biological revolution, if we use it wisely and well, will lead to new methods of prevention and treatment of those parasitic diseases that drain the energy of the peoples of this world and destroy their will.

That concludes my remarks, Senator.

PREPARED STATEMENT

Senator Andrews. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. RICHARD M. KRAUSE

Our work at the National Institute of Allergy and Infectious Diseases (NIAID) is concerned with the microbes that invade us and the immune system that defends us. One of our primary missions is to devise new methods of prevention -- novel types of vaccines, for example. But in addition, we must develop new and more effective treatments because invading bacteria, parasites, and viruses may elude both our natural defenses as well as the immune barrier produced by vaccines. New drugs are an important part of this strategy.

Each of us has an immune system that assures survival in a hostile microbial world, but this system can be a two-edged sword. Protection is the benefit, but allergic and immunologic diseases are sometimes the price we pay. Allergies and many other common diseases, such as certain forms of arthritis, lupus erythematosus, and perhaps even a type of diabetes, result from abnormal immune processes. Many of our scientists are working to discover new ways to repair and regulate the immune system to correct these destructive processes. The means to do so is one legacy of the biological revolution now on our doorstep. This revolution -- based on new and exciting developments in recombinant DNA and hybridoma technologies and in our mastery of the immune system -- will have an ever-increasing impact on most areas of medicine. Because of the promise of this research, I believe we will soon be able to slow the spiraling cost of health care.

Nearly one third of all patients who seek medical care from a physician do so because of infectious, allergic, or immunologic diseases -- diseases for which NIAID has the primary Federal research responsibility. These illnesses that frequently cause morbidity, as well as those that cause mortality, fuel the escalating cost of health care. Because of this, we give high priority to strategies to prevent common diseases.

Infectious Diseases

Infectious diseases remain one of the major health problems of this country and one of the leading causes of absenteeism from work and school. A recent DHHS publication estimated at least 156 million days lost from work each year. The cost for treatment and lost productivity is at least $24 billion.

In order to combat infectious diseases, this Institute supports basic and clinical research, much of it in the area of prevention. In fact, we have been in the disease prevention "business" for decades. Long ago we learned that immunization was one of the most cost effective ways to ease the burden of infectious diseases upon our society. In recent years new successful vaccines for meningitis, pneumonia, rabies, measles, and rubella have encouraged us to intensify our efforts in vaccine development. Moreover, the biological revolution has completely transformed our strategy to develop vaccines -- opening opportunities that we would never have dreamed possible just a few years ago. Because of these opportunities, we have launched a special program for the "accelerated development of new vaccines."

The impact of the biological revolution on vaccine development is illustrated by recent research on a vaccine for hepatitis B. This disease is transmitted by close personal contact between patients and the majority of the population which is susceptible. In addition, persons in certain occupations, such as dentists and health care workers, are at particularly high risk. The first effective vaccine against hepatitis B was licensed by the FDA in 1981. This "first generation" vaccine resulted from collaboration by investigators at the NIAID, other institutes of the NIH, other Federal agencies, universities, and industry. Because we still cannot grow the hepatitis B virus, the virus used in the vaccine must be salvaged from blood of chronic hepatitis B carriers. There are drawbacks to this procedure. The laborious manufacturing process takes 65 weeks, and the necessary three-shot series may well cost at least $150 to $200, a price beyond the reach of many potential users.

Through the wizardry of the new technology, we are already working on a "second generation" hepatitis B vaccine. Using recombinant DNA techniques and other new chemical processes, scientists have synthesized the hepatitis vaccine, bypassing the need for huge quantities of infected blood, the source of the current vaccine. Institute scientists are testing one such vaccine in animals. These new methods open up the possibility of producing pure synthetic vaccines for many other diseases, including sexually transmitted diseases, meningitis, influenza, respiratory diseases of children, and pseudomonas infections in patients with cystic fibrosis.

To help combat sexually transmitted diseases, investigators are pursuing two different vaccines for gonorrhea. One type contains fragments called pili, the hair-like appendages that protrude from the surface of the gonorrhea organism like bristles of a brush. The other is derived from the bacterium's outer membrane protein, a substance called POMP. Both vaccines are being evaluated in volunteers.

More basic research is necessary before a genital herpes vaccine can be developed. Until we have such a vaccine, we must learn more about the epidemiology of the disease in order to improve prevention strategies through new public health measures. Research indicates that the antiviral drug acyclovir is very specific for the herpesvirus. Although acyclovir may not turn out to be the ultimate cure, NIAID studies have shown that this drug rapidly diminishes the shedding of virus from patients with genital herpes lesions. It may be useful, therefore, in reducing the transmission of infection between sexual partners.

Tropical Medicine and International Health

Many developing countries are caught in a trinity of despair -- disease, hunger, and insufficient resources to support growing populations. All this may seem far away and irrelevant to the health of our people. But we are one world. The tide of this despair swells upon our shores and will not recede until we recognize that health for all means wealth for all.

Parasitic diseases such as malaria and schistosomiasis sap the strength and energies of 500 million of the world's poor. Severe viral diarrhea and malaria are among the most common causes of infant and childhood death in many developing countries. The causes of these diseases are known. It is urgent that we find methods to prevent and treat them.

The development of a malaria vaccine is now underway through the application of hybridoma technology. In addition to a vaccine, new strategies to prevent the transmission of malaria include the control of mosquito breeding by altering fertility and sexual habits.

Another major advance has been made toward protecting the lives of the millions of children who die each year from rotavirus infections that cause severe infant diarrhea. Our scientists have been able to grow the human strain of this virus. This was a key discovery that has led to current trials of a vaccine to prevent this disease.

Diseases of the Immune System

As I mentioned earlier, mastery of the immune system could be one of the greatest achievements of the biological revolution. It has been only in recent years that scientists recognized the existence of an immune system -- a whole-body network that includes white blood cells, lymph nodes, spleen, tonsils, thymus gland, and bone marrow. This network consists of approximately 1 trillion specialized cells, called lymphocytes, which are divided into many different sets and subsets, each with a different job to do. Some enhance immune responses, some dampen immune responses, and others have the sole function of killing enemy cells, such as cancer and virus-infected cells. When working properly, the immune system is much like a finely tuned orchestra. The different sets of lymphocytes, working together in health and harmony, serve as a system of checks and balances to regulate immune processes. Immunologic disease occurs when there is an imbalance in these interrelationships.

Using new technologies researchers can now grow each kind of lymphocyte in the test tube. They can study its characteristics with the aim of learning how to restore balance to the immune system and achieve a healthy state. The objective of current research is to prevent or treat immunologic diseases by manipulating the components or products of the immune system. Already there has been success in new forms of treatment for vasculitis, a severe and often fatal inflammatory condition of blood vessels caused by abnormalities in immune function.

Because the immune system is somewhat immature in the very young and sluggish in the elderly, these population groups are especially susceptible to infectious diseases; and current vaccines may not produce protective immunity. More research is needed to develop ways to enhance the beneficial effects of vaccines in the young and old.

Asthma and Allergic Diseases

The prevention of asthma and other allergic diseases is the ultimate aim of a large portion of the Institute's work. One major goal is the prevention of recurrent flare-ups of allergic symptoms that lead to chronic asthma.

We are learning more about the mechanisms of allergy. About 15 years ago scientists discovered a special allergy antibody, called IgE, in the blood of individuals sensitive to allergic substances like ragweed pollen or animal dander. These mischievous antibodies are at the source of the miseries of patients with allergies. They bind to specialized cells that are clustered in the affected organs -- the skin, nose, lungs, and gastrointestinal tract, for example. As a consequence, toxic chemicals, such as histamine, are released. These chemicals cause inflammation and the other symptoms of allergy.

While antihistamine drugs can be helpful, we now know that they are only partially beneficial because other natural toxins are released during an allergic attack. Recent research revealed that a component of cell membranes, called arachidonic acid, is a precursor agent of the leukotrienes -- newly identified substances 1,000 times more potent than histamine in causing the inflammation that occurs in allergies. Institute-supported scientists are trying to find ways of neutralizing the toxic effects of arachidonic acid. Drugs specifically designed to do this could be 1000-fold more effective than currently available antihistamines in the treatment of allergies.

Striking advances have been made in treating certain allergies, including the development of safe and effective allergy shots for sensitive individuals who may experience potentially fatal shock reactions to bee and wasp stings. Much has been done for patients with hay fever and seasonal asthma by improving the chemical contents of allergy shots. And, thanks to continuing basic research, new opportunities are on the way. Some Institute-supported scientists are working on ways to regulate the immune system by suppressing production of the IgE antibodies that trigger the allergy attack.

Basic Research

I would like to conclude with a few remarks on the importance of basic research. Because there are many pressing needs of practical importance, it is often necessary to focus our research on areas of proximal rather than distal promise -- where the gains may exceed the pains, as it were. Examples include the development of new vaccines and new drugs. There is no doubt that such applied research is important. Yet I believe we must do more than that. The Institute must cast a wider net and search where the immediate payoff is less obvious, where the pains may exceed the gains. We must be prepared to travel apart from the beaten path, and leave the comfort of convention. So often, this indirect approach turns out to be the quickest way to solve a problem that eludes a direct attack. Let me cite an example.

Some years ago, a young physician and bacteriologist by the name of Hamilton Smith received a research career development award from the NIAID. His research was concerned with the viruses that infect E. coli, the common bacterium that inhabits the large intestines of people and most animals. What an impractical piece of research that appeared to be at the time. One could have asked, "Why should NIAID support research on viruses that infect bacteria when there was a horde of human virus diseases still out of control?" But what came out of Dr. Smith's apparently "impractical" work was the discovery of restriction enzymes, research for which he received the Nobel Prize in Medicine in 1978. Restriction enzymes are not some esoteric discovery deserving of the golden fleece. Not at all. Indeed, the commercial production of restriction enzymes has become a profitable business because they are essential for the performance of the recombinant DNA techniques applied throughout medical research, industry, and agriculture. We need such boldness as Dr. Smith's, to cut through the brambles of ignorance, if we are to comprehend the nature of health and disease and extract from our gains the means to overcome infectious and immunologic diseases.

This concludes my prepared statement. The budget request for FY 1983 is $246,043,000. I would be pleased to answer any questions.

BIOGRAPHICAL SKETCH

Name: Richard M. Krause, M.D., D.Sc.

Position: Director, National Institute of Allergy and Infectious Diseases

Birthplace and Date: Marietta, Ohio
January 4, 1925

Education: Marietta College - B.A. 1947
Case Western University School of Medicine - M.D. 1952

Experience:

1975 to present	Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
1968 - 1975	Professor, Rockefeller University and Senior Physician to the Hospital, New York
1966 - 1968	Associate Professor, Rockefeller University, and Physician to the Hospital, New York
1965 - 1966	Professor of Epidemiology and Professor of Medicine, Washington University School of Medicine, St. Louis, Missouri
1962 - 1965	Professor of Epidemiology and Associate Professor of Medicine, Washington University School of Medicine, St. Louis, Missouri

1961 - 1962	Associate Professor, Rockefeller Institute, and Associate Physician to the Hospital, New York
1957 - 1961	Assistant Professor, Rockefeller Institute and Associate Physician to the Hospital, New York
1954 - 1957	Assistant, Rockefeller Institute, and Assistant Resident Physician to the Hospital, New York
1953 - 1954	Assistant Resident, Ward Medical Service, Barnes Hospital, St. Louis, Missouri
1952 - 1953	Intern, Ward Medical Service, Barnes Hospital, St. Louis, Missouri
1950 - 1951	Research Fellow, Department of Preventive Medicine, Case Western University School of Medicine, Cleveland, Ohio

Commissioned Corps, USPHS

1977 to present	Assistant Surgeon General
1975 - 1977	Surgeon

Societies and Organizations:

American Academy of Allergy
American Academy of Microbiology
American Association for the Advancement of Science
American Association of Immunologists
American College of Allergists
American Epidemiological Society
American Rheumatism Association
American Society of Biological Chemists
American Society of Clinical Investigation
American Society for Microbiology
American Thoracic Society
American Venereal Diseases Society
Association of American Physicians
Harvey Society
Infectious Diseases Society of America
Institute of Medicine, National Academy of Sciences
National Academy of Sciences of the United States of America
New England Society of Allergy
Practitioner's Society of New York
Royal Society of Medicine
Sigma Xi
Washington Academy of Medicine

Awards and Honors:

1982	Fellow, American Association for the Advancement of Science
1981	Honorary Doctor of Science Degree, Medical College of Ohio, Toledo, Ohio
1981	C. William O'Neal Distinguished American Service Award, Marietta, Ohio

1980	Republic of Egypt Order of Gumhuria Award
1979	Honorary Doctor of Science Degree, Rochester, New York
1979	DHEW, Distinguished Service Medal
1978	Honorary Doctor of Science Degree, Marietta College, Ohio

Religious Affiliations:

Madison Avenue Presbyterian Church, New York, New York
First Religious Society, Marietta, Ohio

Clubs:

Century Association, New York City, New York
Cosmos Club, Washington, D. C.

Editorships

1976 - 1978	Editorial Board, Clinical Immunology and Immunopathology
1976	Advisory Editor, Journal of Experimental Medicine
1974 - 1975	Section Editor, Viral and Microbial Immunology, Journal of Immunology
1973 - 1975	Editor, Journal of Experimental Medicine
1973	Editorial Board, Immunochemistry
1970 - 1978	Editorial Board, Infection and Immunity
1969 - 1973	Editorial Board, Bacteriology Reviews
1963 - 1971	Associate Editor, Journal of Immunology

Other Appointments:

1978	Member, Steering Committee of the Biomedical Sciences Scientific Working Group, World Health Organization
1977 -	The Albert Lasker Medical Research Awards Jury
1977 - 1977	Member, Board of Directors, Lupus Foundation of
1976 - 1977	Member, Board of Directors, Asthma & Allergy Foundation of America
1973 - 1975	Directors Council, New York Heart Association
1973 - 1975	Treasurer, Royal Society of Medicine Foundation, Inc.
1971 - 1977	Board of Directors, Royal Society of Medicine Foundation, Inc.
1970 - 1974	Member, Infectious Disease Advisory Committee, National Institute of Allergy and Infectious, Diseases, National Institutes of Health
1969 - 1971	Chairman, Advisory Council on Research, New York Heart Association
1968 - 1972	Deputy Director, Commission on Streptococcal and Staphylococcal Diseases, United States Armed Forces Epidemiological Board
1967 -	Consultant and Member, Coccal Expert Committee, World Health Organization
1967 - 1973	Board of Directors, New York Heart Association
1966 - 1970	Member, Policy Committee, American Heart Association
1966 - 1970	Chairman, Allergy and Immunology Study Section, NIH

1963 - 1972	Member, Commission on Streptococcal and Staphylococcal Diseases, United States Armed Forces Epidemiological Board
1963 - 1966	Member, Research Committee, American Heart Association
1963 - 1966	Chairman, Research Study Committee, Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association
1963 - 1966	Member, Executive Committee, Council on Rheumatic Fever, American Heart Association

COMMON GENE MATERIAL

Senator ANDREWS. Thank you, Doctor, for a most interesting presentation. I am down here instead of up in the Budget Committee where Mr. Stockman is appearing this morning and where the television cameras are and all of that, and I am quite convinced that what we are doing down here is probably far more important than what they are doing up there although that may get more headlines. And I thought it might be fun to be here because the sense of frustration in dealing with Mr. Stockman knows no bounds, at least for me.

But now you have me frustrated again because you reminded me of a situation we had in the late 1960's when the corn crop in the United States had a common gene because it used common genetic material. I think at that point in time 45 to 50 percent of the corn planted in the United States had that common gene. It was the fastest growing and most drought resistant. We were struck by a disease which attacked this gene and wiped out enough of the U.S. corn crop to really decimate our ability to fill overseas orders and a whole host of other things. If the breeders hadn't been able to react swiftly to it, we would have had a calamity in our normally ongoing, very productive agriculture.

At that point in time, Chairman Whitten and myself, as the chairman and ranking member of the committee to fund the Department of Agriculture, set up what we thought was a system, in the interest of the people, to make sure we had differentiated germ plasma throughout the major crops like corn and wheat. I am reminded now that that worked for 2 years. We have promptly forgotten about it—the Government has promptly forgotten about it—and I am concerned that we are now back in the same state where our major cereal crops are produced with a common germ plasma which makes them very susceptible to a type of virus or plant disease that can come along.

Your presentation today again reminded me we have to address ourselves to that problem as well as the problems you're talking about, because in helping people survive disease, they have to have good diets. And the supply of food is extremely important in providing adequate nutrition so that they can be healthy.

It's all tied together. Sometimes we think we are solving our problems, and then we find there are five more coming down the pike.

Your budget proposes to cap, Doctor, indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 4 percent and maintain training allowances slightly below the fiscal 1982 level. What will these policies do to your research and training efforts?

IMPACT OF REDUCTIONS IN GRANTS AND TRAINING

Dr. KRAUSE. Well, I think my answers would follow along similarly to those that Dr. Goldstein has given.

There is no doubt that, as there are somewhat less funds available to individual investigators, overall work will be slowed.

I think, however, what will be important for us as science managers is to be sure that the key and cutting edge areas are funded as fully as possible.

Science advances on a broad front. But there are certain very sharp and penetrating points. It is important that we do all we can to identify those and be sure that they receive all the support that's possible.

On the other hand, it should always be recognized that some of the greatest advances come "apart from the beaten path."

I just talked to you about the hepatitis vaccine. The initial discovery was made by Dr. Blumberg who received the Nobel Prize, and he was not looking for the hepatitis vaccine at all. He was doing something entirely different. And yet, out of what he was doing came this marvelous vaccine.

So there is no doubt that the pace of the undirected work, the work that is exploring the unanticipated, will be slowed by this budget reduction.

ABILITY TO PRODUCE GOOD SCIENCE AND RESEARCHERS

Senator ANDREWS. Similar to the question I asked Dr. Goldstein, what will it do to the ability of grant recipients to produce good science and good researchers?

Dr. KRAUSE. I think that they will need to be somewhat more selective in the experiments they do. A little selectivity is perhaps sometimes a good thing.

Up until a few years ago, Senator, I was running a laboratory in one of the eastern universities, Rockefeller University. One of the first things one would do in response to a budget cut would be to take on one or two fewer younger people. That is one way one can cut back costs in the lab roughly 10 percent or so.

DEMAND FOR TRAINED RESEARCHERS FOR INDUSTRY AND AGRICULTURE

Senator ANDREWS. But what does that do to your pool of trained researchers 10 years down the pike?

Dr. KRAUSE. That means 10 years down the line we will have fewer researchers.

And I think in that connection let me say—and it's not yet been brought out in these hearings—I believe that 10 to 20 years from now the demand for trained people for industry and for agriculture will be far beyond any that we are anticipating at the moment.

I have been told by the executives of Dupont, that less than 5 percent—and this is published information, not private—of their current income of some $20 billion is from biological products. But in making long-range plans, they expect that in 15 years over 50 percent of the profits will be from biological products produced by the biological revolution.

I think the largest demands for biomedical scientists that we train in the future, unlike the past, will be for industry and agriculture.

Senator ANDREWS. Doctor, if industry and agriculture takes from you your trained researchers, if they take the ones with experience, wouldn't that leave you more room to bring in new ones? To what extent can you keep training new ones, and how important is it to your operation to retain a cadre of well-trained professional researchers?

Dr. KRAUSE. Well, it is important, of course, that we constantly have a flow of young people coming into our laboratories. That's where the new ideas come in; that's where the new minds generate the excitement; that's where the ferment is.

And I think what I really was trying to say is that the NIH, through its training programs around the country, is the greatest supporter of training for the biological sciences in the United States. And the people that will be trained in this system—and, therefore, we must continue to nourish large numbers coming into it—will be graduating and going, not into the conventional career opportunities as in the past, which have been primarily into the universities, but also into industry and into agriculture.

Senator ANDREWS. With the pay cap that seems interminable around here, doesn't that mean that in a sense you become almost more a training ground providing these researchers for corporations rather than a research group yourself?

Dr. KRAUSE. I think that that is a serious problem.

Senator ANDREWS. Isn't that threatening? I think probably I should pose it another way: Doesn't that threaten your operation because you become more a training ground for corporations who can pick up these people with experience? As a result, isn't your ability to conduct research somewhat diminished?

Dr. KRAUSE. I think that you have touched an important point, and that is that at the middle level of our faculty, if I may call them that—because I think of them as faculty—at the middle level our salary, and at the senior level, which would be the equivalent to the full professor level, our salary and other compensations do not compete with the better universities or now with what the new industries are prepared to pay these individuals.

Fortunately, sir, the income of our younger people, I believe, is still competitive with the universities, and so I am pleased to say that at least in our own Institute, and I think for all the Institutes, we are still competing very well for the young people that have equal opportunities to go to Harvard or Cal Tech or MIT or the other great universities of the country.

IMPACT OF 1982 CONTINUING RESOLUTION

Senator ANDREWS. Doctor, what has been the impact of the 1982 continuing resolution which imposed, as you know, the lower of the House and Senate figures, or a 4-percent reduction beyond that?

Dr. KRAUSE. Well, first of all, we had a 4-percent reduction in all grants which I spoke to you about. Almost 65 percent of our budget goes to individual research grants.

We have also reduced the number of contracts. Let me say a word about that. Our contract budget is really very small, and the contracts are, of course, what we use to test new vaccines and to carry out other applied research of that nature.

It is an important part of the continuum of science from the basic work at the laboratory to the work at the bedside and to the final product that can be used generally for the health of the American people. There is an important area of practical and applied research that we must do before it is picked up by industry and we have had to reduce some of that contract activity.

Finally, we have had to completely eliminate all competing awards of grants that are difficult to explain, but are very important. They are called research career development awards. These are awards of 5 years of support for mid-level investigators, to hold them in science rather than have them range out into the richer pastures of practice, to hold them in science with a reasonable salary paid by these research career development awards.

Some of the Institutes have been able to continue these programs and they have sparked clinical investigation. We have had to eliminate all competing research career program awards and as a result it is fair to say that clinical investigation in infectious diseases and allergy in many of our medical schools has lagged way behind the other subspecialties of internal medicine. For example, there are only three medical schools in the country with centers that specialize in sexually transmitted diseases, and we in this room all know that this is a group of diseases that is now rampant and epidemic in this country.

So these are the ways in which this has had an influence on our programs.

RESPONSE TO DIRECTIVE ON SEXUALLY TRANSMITTED DISEASES

Senator ANDREWS. In fact, Doctor, in our fiscal 1982 report, the committee expressed some intent that the Institute should maintain, if not strengthen, research on these sexually transmitted diseases. It also noted the Institute would be expected to coordinate its work with the STD prevention and control activities of the Centers for Disease Control.

What has been your response to this directive?

Dr. KRAUSE. Our response is that we have—these flip charts were made so that I am supposed to be able to find things more rapidly, but it doesn't work out that way. [Laughter.]

Our response has been, sir, that despite the continuing resolution, we will nevertheless increase our expenditure for sexually transmitted diseases, other than genital herpes, by $200,000. We spent $9.4 million in 1981; we anticipate spending $9.6 million in 1982, this current year. For genital herpes we expect to have it increase another $100,000 in fiscal year 1982. So we have at least maintained and perhaps given some extra attention to the program.

The other important thing that we have done concerns the use of the new marvelous ambulatory care research facility for sexually transmitted disease research on patients. One of the first decisions that Dr. Sell made—and I think it was, in fact, one of the first clinics to open up in that new ambulatory facility—is that we would have a sexually transmitted disease clinical investigation program in that new facility. It is concentrating on herpes and on other viral diseases. And so we have increased our activity in the intramural program to cover this.

Furthermore, let me say that one of the new laboratories established in the reorganization of the Rocky Mountain laboratories was a laboratory that is concerned specifically with the problems of sexually transmitted diseases.

SUPPORT FOR SEXUALLY TRANSMITTED DISEASE RESEARCH

Senator ANDREWS. $200,000—you know, to those of us back on the farm, that's a lot of money, but in the years I have been down in Congress I am reminded of Everett Dirksen's statement that $100 million here and $100 million there adds up to real money.

Isn't this just kind of a drop in the bucket as far as the need is concerned with this rampant increase in the level of this disease across our country?

Dr. KRAUSE. Well, there is no doubt that this problem needs more attention than it is now receiving.

Senator ANDREWS. What percentage increase does this amount of additional funding give you in your work against this disease? Could you express it in those terms? I think it would be more meaningful for the record.

Dr. KRAUSE. I'm sorry. What was the question again, sir?

Senator ANDREWS. What percentage of increase in activity in your work against this disease does this increase in dollars amount to?

Dr. KRAUSE. The $300,000 increase in fiscal year 1982 is only 2 percent; but we estimate a further increase of about $500,000 in fiscal year 1983 which is roughly between 3 and 4 percent.

Senator ANDREWS. So the increase has resulted in only a 3- to 4-percent increase?

Dr. KRAUSE. Yes; but I think it's important to realize that we've done two things. We have established not only a new operation on the main campus, but also a new laboratory devoted to this problem at the Rocky Mountain laboratories. And both will be new training grounds. These are the new training grounds for the young people. We have extremely bright, able senior investigators who have been selected, have been recruited, to run these programs and they, in turn, are recruiting bright young people.

And I see in the next few years, once these younger people move out into the universities and establish their own programs, a wider effort in this program will follow.

Senator ANDREWS. So the type of program you have designed should give us a much greater impact than the mere percentage of increase dollarwise?

Dr. KRAUSE. That is correct.

Senator ANDREWS. You can expand on that for the record, too, Doctor.

[The information follows:]

SUPPORT FOR RESEARCH ON SEXUALLY TRANSMITTED DISEASES—STD

In addition to the $300,000—2 percent—increase in research on STD and, of that amount, the $100,000—3 percent—increase in genital herpes research in 1982, I think it is very important to consider our additional efforts in this disease area.

In March 1980, the intramural laboratories of NIAID that are located in Hamilton, Mont., were reorganized into three separate research laboratory components. One of these, the Laboratory of Microbial Structure and Function, now has a program on the study of Neisseria gonorrhea and chlamydia organisms, both prominent causes of STD in the United States. This laboratory is utilizing modern molecular biology and recombinant DNA research to investigate interactions between the STD organisms and the host immune defense mechanisms. While the laboratory's primary mission is the understanding of bacteria-host interactions, it is anticipated that this knowledge will uncover the most promising antigens of the STD bacteria that can then be used to develop potent vaccines. Over the past 2 years this laboratory has grown with the recruitment of eight additional junior scientists. The Laboratory of Microbial Structure and Function, with its modern biomedical research capability, is expected to have a substantial impact on our understanding of sexually transmitted diseases.

The construction of the Ambulatory Care Research Facility on the Bethesda campus of the NIH has allowed the NIAID intramural program to expand its research related to the current national epidemic in sexually transmitted diseases. Dr. Stephen Straus, head of the Virology Section of the Laboratory of Clinical Investigation, is studying virally caused sexually transmitted diseases. He already has begun the study in his clinic of antiviral agents—Acyclovir—for the control and possible treatment of infections such as herpes 2. The research staff is also studying other STD viruses including the more recently identified problem of cytomegalovirus in STD.

It is also important to consider the training programs at the intramural laboratories. One of the major recommendations of the 1980 STD study group's 5-year projection is that of increased support in training. NIAID laboratories are actively training young scientists in highly sophisticated techniques and approaches to solving STD problems.

These are but two examples that should have a major impact on progress against STD's beyond what might be expected with the proposed funding increase.

HEPATITIS B VACCINE

Senator ANDREWS. Another field: How soon can we anticipate the hepatitis B vaccine to be available for general use? I understand Food and Drug cleared it on November 16.

Dr. KRAUSE. The last conversation I had with Merck is that they expect to have it available this summer.

STATUS OF INTERFERON RESEARCH

Senator ANDREWS. This summer.

What is the current status of your research on interferon?

Dr. KRAUSE. Interferon research——

Senator ANDREWS. We heard that it was the great cure-all and now lately we have been hearing it's not quite as effective as we were led to believe it might be.

Dr. KRAUSE. Well, I think that interferon probably will be discussed again by Dr. DeVita, but let me try to put it in some sort of——

Senator ANDREWS. How does your research—and that's why I wanted to get the question before he came—in this field relate to the research of the National Cancer Institute? Are you doing it? Are they doing it? Are you doing it together?

Dr. KRAUSE. First of all, we are doing it together. There's very, very close liaison between what the two Institutes do on this program. In fact, we will even collaborate on the same projects in which some of our investigators and theirs will work together.

We are using it specifically to see if it might not be effective in genital herpes in women. Those clinical trials are underway.

We, of course, would like to prevent all hepatitis with the vaccine, but that is not yet possible, so we are using interferon with other antiviral drugs to see if we can cure patients who have hepatitis.

We are also working closely with the Cancer Institute on delineating or defining what interferon is. I suspect, in the end, until we know a good deal more about what it is and how it works, we will not have the final answers as to the effectiveness of interferon as an antiviral drug.

But I would say this about interferon. Let me put it this way: Interferon is a most impressive compound which is now 20 years old. It has profound effects on the regulation of the metabolic processes of the cell, particularly the processes of cell division. And I believe when we understand what this new class of compounds does to the physiology of the cell, we will have a much better idea on how to use interferon and its products to treat disease.

SUBMITTED QUESTIONS

Senator ANDREWS. Thank you very much, Doctor, for your most interesting testimony. We, of course, have some additional questions that we will give you to be answered for the record, and the subcommittee would appreciate it very much if you could provide those answers at the same time that you return the corrected hearing transcript.

Thank you again very much for sharing your book with us, for bringing along a noted Cass County native. You do all the proper things politically. [Laughter.]

Dr. KRAUSE. Thank you.

[The following questions were not asked at the hearing but were submitted for response for the record:]

Questions Submitted by the Subcommittee

BUDGET

Question: How will the proposed budget affect your program planning for the coming year?

Answer: We anticipate intensifying our program planning activities during 1983. In recent years the NIAID has convened four groups of scientists to identify areas of need and scientific opportunity within the broad area of our responsiblility. The National Advisory Allergy and Infectious Diseases Council reviewed the work of the Task Forces and made programmatic and funding recommendations to the NIAID. The Institute is examining alternative plans for reassessing our program opportunities, balance, and scope in the light of current fiscal constraints.

Question: Where will you place your priorities?

Answer: Our overall priorities will remain unchanged, as they are presently set to maintain the scientific excellence of the programs while at the same time fully meeting the goals of the Institute's mission. We do not plan to change the balance between the extramural Microbiology and Infectious Diseases Program and the Immunology, Allergic and Immunologic Diseases Program. Over recent years that ratio of funding has been approximately 60:40, and we plan the same distribution for 1983.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: We have always felt that free-ranging, investigator-initiated research was the cornerstone of our research programs. These individual research project grants will continue to be emphasized because we believe that such innovative research is essential to the removal of the barriers hindering progress to the successful diagnosis, prevention and treatment of disease. In order to maintain a supply of scientists who are well equipped to staff the laboratories of the future we have also viewed the training programs as vital to the long-range scientific endeavor. Both of these areas have been receiving special attention during the budget formulation process which assures careful consideration each year. The combined effects of budgetary restrictions and inflation have caused us to make reductions in other important but slightly lower priority areas, including our contract programs and the Research Career Programs.

GRANTS COMPARISON

Question: Please explain why you plan to make the following reductions in your competing research grants:

--New -- From 213 in FY 82 to 161 in FY 83.
--Renewal -- From 172 to 131.

Answer: We continue to place top priority on research project grants, but we also believe that support for the other programs should not erode further as a proportion of the budget because these mechanisms are essential for translating the results of basic research into treatment and prevention modes for developing crucial kinds of research expertise and resources.

In addition to our concerns regarding program balance in a period of fiscal constraint, the number of research project grants we expect to be able to fund will decline because of such factors as the following: the rapidly increasing average cost of research project grants from year to year; the need to support ongoing grant commitments at increased average costs; and expectations to fund additional large program projects, which require a more substantial investment than the smaller research grants.

Question: At the same time you are cutting back on competing grants, you are increasing intramural research by $4 million and research and development contracts by almost $3 million. What is the reason for this?

Answer: Most of the increase for intramural research reflects mandatory increased costs of salaries, centrally furnished services, and supplies and materials. The program increase for intramural has been requested, in part, to take advantage of an emerging, exciting technical approach to vaccine development which may make it possible to provide protection against a wide variety of infectious diseases at low cost. Also, in their FY 1982 report, the Senate Appropriations Committee expressed its concern "that the Institute maintain, if not strengthen, its research on sexually transmitted diseases (STD)." The Institute's strategy on STD research has led to plans for new emphasis by two intramural facilities. Thus, part of the increase will be used to provide an additional biochemistry capability for the laboratory in Montana that is devoted to understanding the interaction between the bacteria that cause STD and the hosts they invade. Additional resources will also be directed toward the development of a new outpatient program for the study of STD's caused by viruses. The remaining funds will be devoted to initiating innovative forms of treatment for lupus and other immunologic diseases.

Research and development contracts are used by this Institute to develop new methods of prevention and treatment from the knowledge acquired through basic research. Contract activities include vaccine development and clinical trials, which are critical components of NIAID's Disease Prevention Program. The requested increase in funds will be used to support these efforts. While the 1983 budget reflects an increase for R & D contracts over 1982, it should be noted that R & D contract support has declined from a level of $16,240,000 in 1978, and the requested level of $13,403,000 will not support all ongoing contract activities.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982 and how much will you spend in fiscal 1983?

Answer: In 1982, NIAID plans to support 20 research centers with estimated funding of $4,600,000. The 1983 budget request includes $5,127,000 for support of 20 centers.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: Each center has a core administration budget. By coordination of all the projects through the core administration, economies have already been effected by eliminating duplication of resources and staff. Beyond that, only essential research and treatment activities are funded with the exception of certain "outreach" activities (in the Centers for Interdisciplinary Research on Immunologic Diseases) designed to carry out technology transfer. While only a very small percentage of the budgets of these centers is allocated to such activities, which include education of the community and teaching of self-management of asthma to children, these programs could be cut back without impairing essential research and basic treatment activities; but an integral part of care, patient education and self-management, would be sacrificed.

TRAINING

Question: In last year's hearings, testimony indicated there was a decline in the number of clinical investigators participating in several Institutes' training programs. The Committee also noted in its FY 82 report that there is a significant shortage of investigators in the field of research on sexually transmitted diseases. The Committee directed you to address itself to this problem. What funds have been set aside for the training of the next generation of research professionals in the field of allergy and infectious diseases?

Answer: NIAID support for research training is estimated at $8,149,000 in 1982; the 1983 budget request includes $8,025,000 for these programs. Funding for research training related to sexually transmitted diseases represents approximately 6 percent of the total training funds.

Question: To what extent will priority be given to training investigators in the field of sexually-transmitted diseases research?

Answer: High priority has been given to training of investigators in the field of sexually transmitted diseases (STD). The NIAID STD Study Group recommended support for the training of the following investigators per year: 200 Ph.D. postdoctoral fellows and M.D. research associates; 300 microbiologists; 50 physicians (clinical fellowships); and 60 student fellowships. Although a special award (K08) was announced for the support of clinical investigators and we have supported training in three STD Research Units, funds have not been available to fully implement these recommendations. A high priority in the new Ambulatory Care Research Facility at the Clinical Center in Bethesda will be research and research training in the field of sexually transmitted diseases. This includes important work on sexually-transmitted viral diseases such as genital herpes, and clinical trials of drugs to treat these diseases.

Question: How can more individuals be encouraged to pursue a career in the areas for which the Institute is responsible?

Answer: There are two key components in attracting an individual to a research career: 1) a role model, and 2) convincing prospects for continuing support, growth and advancement. In the case of clinical investigators, stronger sections of infectious disease need to be created in the Nation's academic medical centers. This has been approached to a very limited extent by supporting a few centers of excellence in special areas; e.g., sexually transmitted diseases, fungal diseases, tropical diseases. As for opportunity for growth, this is best assured by continued Federal support. As one means of encouraging pursuit of a career in the areas for which the Institute is responsible, training program awards are made available to both physicians and basic scientists. In this regard, two funding mechanisms exist, one in which the individual receives the award and the other in which the institution receives and administers the award. Another means of encouraging this career option is through research career program awards, including K04 research career development awards.

Question: Are there non-Federal or non-governmental sources of funding that could be tapped to expand the pool of researchers?

Answer: Limited funds are available from a few special interest groups (American Thoracic Society; Rockefeller Foundation; Cystic Fibrosis Foundation), but potential funding is limited for a general area such as infectious diseases compared to categorical areas such as heart disease and cancer. Industry employs a large number of microbiologists, but supports only a handful of trainees or fellows.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: The 1983 budget request contains only mandatory increases in direct operations and program management. In order to offset increased costs in travel, postage, supplies, printing, etc., we have reduced the use of overtime, restricted the printing and distribution of informational pamphlets and reduced the number of conferences and workshops we support. We have also increased our use of contract airlines and other reduced fares for those trips that we must take to carry out our mission.

Question: What are your most important administrative concerns--and what are your least important concerns?

Answer: All administrative matters are of concern to the Institute particularly during a time of economic restraint. A major concern centers on our inability to rapidly recruit and retain the top quality scientists, physicians, and administrators required to carry out our mandate. We have increased our efforts to control administrative costs in all areas, particularly in travel, equipment and supply purchases, and consultant services without compromising the efficiency of administering our program or the integrity of the review system.

Question: What criteria do you use for determining your administrative priorities?

Answer: The highest priority goes to those areas where we have a legal requirement such as administering grants and contracts. Secondly, we try to comply with Congressional and Departmental objectives. In all areas, of course, we attempt to perform our tasks in the most efficient and effective manner possible, so there are considerations of cost benefit ratios.

INTERNATIONAL BIOMEDICAL RESEARCH

Question: The Institute's International Biomedical Research Program conducts research and scientific training on infectious diseases important to the health of the world's developing countries. The ultimate goal is improved technology for preventing, diagnosing and treating these diseases. To what extent have your efforts with Japan and the Soviet Union been fruitful?

Answer: Cooperative efforts with the Japanese have been highly successful. The U.S.-Japan Cooperative Medical Science Program, initiated in 1965, has been concerned with diseases of substantial health importance in Asian countries. The categories of diseases initially selected for study were cholera, leprosy, parasitic diseases, tuberculosis, and viral diseases, all sponsored by NIAID, plus malnutrition, sponsored by NIADDK, and mutagenesis and carcinogenesis, by NIEHS. For each of the disease categories, ten-member joint panels, consisting of five scientists from each nation, have cooperated in carrying out program activities in three categories: research, joint scientific conferences, and exchange of persons. In the last two years, new panels on hepatitis and immunology have been established. The successful accomplishments of the program are detailed in the recently published Third Five-Year Report, 1975-1980 (Department of State Publication 9127). More recently, under the newly established Joint Committee of Japan-U.S. Cooperation in Research and Development in Science and Technology, cooperative efforts have begun in the area of recombinant DNA.

Influenza is a virus which is subject to change, and these changes sometimes lead to pandemics. The exchange of information and new virus strains with the USSR has been open and useful. Joint meetings and scientist exchanges have been successful in supplying results which would otherwise have taken at least a year through the usual publication methods. An example of this beneficial collaboration was the suggestion by visiting Soviet scientists to use ribavirin (an antiviral agent) by aerosol for the treatment of serious influenza disease. This has proven successful, and further studies are underway. Through the collaborative programs, a complete review of the considerable Soviet experience with another antiviral (rimantadine) has been obtained and published in a U.S. scientific journal.

Question: In what areas of research are you cooperating with other countries?

Answer: Collaboration in international research is carried out by intramural NIAID staff, awards to U.S. universities to conduct research overseas, and exchange research fellowships or direct grants to foreign scientists. Under the International Collaboration in Infectious Diseases Research Program, studies are underway in parasitic diseases or leprosy with collaborating scientists in seven developing countries (Brazil, Colombia, India, Mexico, Nigeria, Sudan, and Thailand). Several new bilateral science and technology agreements established in recent years have called for collaborative activity in tropical medicine, microbiology, and infectious diseases. NIAID intramural scientists are involved in collaborative studies in West Africa (malaria), India (tropical pulmonary eosinophilia), and Brazil and Argentina (American trypanosomiasis). Under the U.S.-People's Republic of China Bilateral Program, studies have begun on hepatitis, and preliminary plans have been developed for collaboration in immunology and selected parasitic diseases. Following the decision by Congress to set aside funds for regional scientific cooperation in the Middle East, support is being provided under an interagency agreement between NIAID and the Agency for International Development for a cooperative research project in Egypt and Israel on the epidemiology and control of arthropod-borne diseases (Rift Valley fever, malaria, and leishmaniasis). Consideration is being given to collaborative studies of diarrheal diseases in India and of leprosy in Venezuela.

Question: How much will this effort cost in fiscal 1983? How much in fiscal 1981?

Answer: In FY 1981 the NIAID obligated $31,250,000 in support of international research activities. Estimated funding for these activities in FY 1982 and FY 1983 is $31.8 million and $33 million, respectively.

RECOMBINANT DNA ADVISORY COMMITTEE

Question: Please provide us with a status report on the proposed revision of the recombinant DNA guidelines.

Answer: The NIH Guidelines for Research Involving Recombinant DNA Molecules are a set of safety standards for this important technique which is of great use in biomedical research and increasingly useful in industry.

All proposed revisions of the NIH Guidelines are published in the Federal Register for public comment, and then discussed at an open meeting of the Recombinant DNA Advisory Committee (RAC) whose 25 members (scientists and laymen) are appointed by the Secretary, DHHS. Following each RAC meeting, the NIH promulgates in the Federal Register those changes in the Guidelines which have been recommended by RAC and which are accepted.

At its most recent meeting, February 8-9, 1982, the RAC rejected a proposed radical revision of the Guidelines, and recommended instead a moderate revision, which would simplify the Guidelines and lower the containment and administrative requirements for certain specified types of experiments. NIH is currently analyzing the RAC recommendation and the public comments it has received. A decision is expected in April.

Question: Has the role of the Recombinant DNA Advisory Committee changed as a result of these revisions?

Answer: The proposed revision would leave the functions of the RAC unchanged.

Question: What will the Committee's future activities involve?

Answer: As in the past, any proposed changes in the NIH Guidelines must be reviewed by the RAC. Also, proposed experiments falling into certain classes specified in the Guidelines must receive RAC and NIH approval before they may be started.

IMMUNOTHERAPY

Question: One of the most important areas of work for the Institute is on the body's immune system. In your fiscal 1982 justifications you stated that "mastery of the immune system...is at hand." You also said that "we are entering a new era," which made us all think that a sort of "Golden Age of Medicine" is upon us. Has all of this been borne out by subsequent developments -- is "mastery of the immune system at hand"?

Answer: Through the use of new and exciting developments in recombinant DNA and hybridoma technologies, many of our scientists are working to discover new ways to repair and regulate the immune system and to correct abnormal, destructive processes resulting in allergies and many other common diseases, such as certain forms of arthritis, lupus erythematosus, and perhaps even a type of diabetes.

In experimental animal models, it has been shown that it is possible to rectify abnormal processes by manipulation of the immune system. Translation of these new therapies into humans is progressing. For example, children with congenital absence of immune system factors can be immunologically reconstituted through transplantation of cultured thymic epithelial cells.

The availability of pure (monoclonal) antibodies generated from hybridomas is permitting a new approach to the treatment of acute lymphoblastic leukemia of childhood. The approach is the destruction of cancer cells by treatment with hybridoma antibodies that are specifically designed to "target in" on the cancer cells. While the abnormal cells are destroyed, the normal cells are spared any ill effects.

Monoclonal antibodies are also currently being used in the diagnosis of certain viral infections. Availability of such diagnostic reagents will allow the rapid diagnosis of such diseases.

We now have the ability to modify the internal processes that regulate the immune system. Such knowledge has been used to improve the results of kidney transplants. It is possible, for example, in the immediate post-transplantation period to detect the rejection process at the very onset. As a consequence with appropriate early treatment the rejection of the transplant can be prevented.

From the new knowledge on the immune system, experimental treatments can be designed for the effective management of patients with immunologic diseases (such as systemic lupus erythematosus and rheumatoid arthritis) characterized by the oversuppression or overstimulation of the immune system.

Question: What are the possible benefits yet to be realized from your accomplishments in the area of immunotherapy?

Answer: Immunotherapy techniques (allergy shots) are designed to lessen reactions on exposure to known allergens. This benefit is, in part, derived from a decrease in IgE (the allergy causing antibody) and an increase in IgG, (the blocking antibody). Chemical manipulation of allergenic extracts used in immunotherapy has been shown to enhance these effects. Reagents about to be licensed for such therapy offer greater therapeutic potential, with fewer shots. Such reagents are also less likely to cause adverse reactions. There are also experimental leads to be followed that show that tolerance can be induced by actually shutting off the harmful antibody production.

SEXUALLY TRANSMITTED DISEASES

Question: In our FY 82 report, the Committee expressed its intention that the Institute should maintain, if not strengthen, research on sexually transmitted diseases. It was also noted that the Institute would be expected to coordinate its work with the STD prevention and control activities of the Centers for Disease Control. What research is being done in the prevention and treatment of sexually transmitted diseases?

Answer: The NIAID has maintained a targeted program on sexually transmitted diseases (STD) research for over a decade. Research supported by this program covers a wide array of STDs: gonorrhea, syphilis, chlamydial and genital herpes infections, trichomoniasis, STD enteric infections, group B streptococcal disease and cytomegalovirus (CMV) infections.

It is important that a thorough understanding of these diseases and their causal agents be clarified so that specific problems relating to diagnosis, prevention, and therapy can be initiated with a greater chance for success.

The research program focuses on the following basic aspects of these diseases:

- biology of the causal microorganisms
- virulence factors of these microorganisms
- role of the host's immune responses
- immunopathology of these diseases
- pathogenesis and mechanisms of resistance, recovery and latency
- animal model systems for study of these diseases
- development of diagnostic methods
- therapy and prophylactic measures (vaccine development)
- epidemiology

The research projects include efforts to develop candidate vaccines for gonorrhea, group B streptococcal infections, and genital herpes. Other investigations underway also include intensive study of the most effective therapies for chlamydial infection and pelvic inflammatory disease, and of several promising antiviral agents for therapy of genital herpes.

Question: How are you coordinating your work with comparable prevention and control activities of the Centers for Disease Control?

Answer: Since the inception of this targeted program, close and cordial relations have been maintained with staff of the Venereal Disease Control Division at CDC. Continued communication by telephone or letter is a regular feature of this coordination. Additionally, CDC members are routinely invited to NIAID workshops, conferences, and concept reviews on specific STD topics. Staff members of the VD Control Division have served as members of site visit teams at reviews of NIH funded STD research centers and have also assisted in reviews of NIH contracts dealing with STD investigations. NIAID staff have also attended a number of workshops and conferences at CDC so that concordance of action on special STD problems could be agreed upon. The working relationship has been a smooth and fruitful one over the years, on both an official and a personal level.

Question: What will your FY 1983 funding level be in this area?

Answer: NIAID support for research and training on sexually transmitted diseases is estimated at $13,324,000 in 1983, an increase of 4 percent over the level for 1982.

Question: In terms of the four most prevalent and serious sexually transmitted diseases -- that is, syphilis, gonorrhea, herpes, and chlamydial infections -- how much actual increase in research efforts has taken place in the last three or four years?

Answer: The increase in support of this program has risen from $8.4 million in 1979, $9.5 million in 1980, and $12.6 million in 1981 to an estimated $12.8 million in 1982. It should be pointed out that, from inception of this program in 1971, support has risen from an initial $100,000 to an estimated level of $13.3 million in 1983.

Question: The American Social Health Association estimates at least 20 million Americans suffer from herpes. How much does the Institute spend to look at this problem as a sexually transmissible disease?

Answer: The Institute supported research on genital herpes at a level of $1.2 million in 1980; $3.2 million in 1981; and an estimated $3.3 million in 1982. Projected expenditures in 1983 are at a level of $3.4 million.

Question: Does this amount seem to you to be an appropriate response to the problem?

Answer: The funds allocated to genital herpes research are at a realistic level, given the overall budgetary constraints at this time. The number of investigators currently involved in this research area is adequate. The major problem in herpes research is a scientific and technological one, meaning that there are still many gap areas in our knowledge of the basic biology of the virus itself, its behavior as a pathogen, and the means needed to prevent or treat the disease. Until additional scientific or technical developments occur, the current program is an appropriate one of support for research on genital herpes.

Question: Do you view herpes as a priority research area for your Institute?

Answer: Research on genital herpes infection is a targeted program of the Institute, in conjunction with the targeted program on the other important STD problems. The Institute also is preparing to support at least one additional research center that is specifically focused on the problem of genital herpes.

Question: Venereal diseases are a growing public health problem. Why do they continue to receive such a small proportion of the Institute's funds and attention?

Answer: The allocation of funds to the STD problem is actually not such a small proportion of Institute resources. It should be noted that the total budget for extramural research support in the Microbiology and Infectious Diseases Program (MIDP) is projected at \$112.2 million. Of this amount, estimates are that \$13.3 million, or 12% of MIDP funds, will be spent on STD research. Additionally, the Institute has established STD research projects in its intramural programs. Study of gonococcal and chlamydial infections is conducted at the Institute's laboratory in Hamilton, Montana, and the Institute's laboratory in Bethesda is investigating genital herpes. There are many other diseases of significant public health importance that also merit Institute support for research; a balance must, therefore, be sought for support of all these areas.

Question: What effort does the Institute make to seek out applicants to work and train in this area of research?

Answer: Institute program staff initiated this targeted STD program; at the same time they stimulated investigators to make this research area a rewarding career field. The field no longer requires additional programming efforts to entice trained research workers in the basic aspects of these diseases. There is, however, a distinct lack of trained clinical investigators for studies oriented toward clinical problems. Additional training programs are needed to increase the number of clinical investigators in this area.

Question: Will there be any training grants awarded in sexually transmitted disease research this year?

Answer: There will probably be no new training awards in STD research in 1982. Owing to decreased funds for continuing training programs, STD research training, as well as training in immunology and infectious diseases, is at a low level. There is a pronounced lack of new applications requesting support for training programs in this area, both by individuals and by more formal departmental (institutional) training programs. This situation is expected to change when additional training funds are available.

Question: Venereal diseases have always been a difficult topic to discuss. Do you think this attitude exists even within the research establishment?

Answer: There is no difficulty within the research establishment regarding free and spirited discussions of the problems of STDs. One has only to attend a major scientific meeting when a session is devoted to an STD topic to see this. It is gratifying to observe the large numbers of scientists of many backgrounds freely discussing these problems.

Question: What impact does this have on research?

Answer: There is a very positive effect on research, owing in large part to past efforts by the Institute to initiate the STD program and to make scientists aware of it. Many worthwhile research proposals continue to flow into the National Institutes of Health for review. The momentum built up in the past will undoubtedly continue, so long as the Institute provides research support and there is a perceived need that this is a major public health problem in need of resolution.

Question: How many teenagers have a venereal disease?

Answer: There is very little hard data available on which to base a firm answer. The latest information from the Centers for Disease Control indicates that there were about 1 million reported cases of gonorrhea, with an estimated 2 million actual cases overall for the total population. Approximately 26% of the cases of gonorrhea in 1980 were teenagers.

The numbers of cases of nongonococcal urethritis in teenagers were approximately the same as for gonorrhea. Genital herpes tends to be more prevalent in a somewhat older age group, ranging from the early twenties to the mid-thirties. Syphilis likewise tends to occur in the same age group as genital herpes, so that teenage cases of this disease would also be smaller. No specific data are available.

Question: How many infants suffer from venereal diseases?

Answer: It was estimated by the NIAID Study Group on Sexually Transmitted Diseases that approximately 30% of all infants are infected with an STD organism. Only about 100,000 infants per year, however, have overt disease as a result of such infection. The chief disease problems in this population were cytomegalovirus, chlamydial infections, herpesvirus infections, and group B streptococcal infections.

Question: Do you believe that venereal diseases present a serious enough problem to the nation's health that the Institute might look toward a re-ordering of its research priorities to make a determined effort at controlling these diseases?

Answer: There is no question regarding the magnitude of the STDs as a public health problem. We believe it would be a serious error, however, to reorder Institute research priorities for this one problem while neglecting other equally serious public health problems that the Institute must attack. The Institute is responsible for research support on a wide array of infectious and allergic diseases; attack on one problem should not preempt efforts on other problem areas. Internal readjustments have already taken place to support research efforts on the STD problem to the significant extent already underway.

Question: Why can't you undertake a major effort with the funds you already receive?

Answer: The Institute's effort is already a major one devoted to this public health problem. Every effort is being made to attack the problem with the funds available. Any significant expansion of effort beyond what is already being supported would require additional funding.

HEPATITIS VACCINE

Question: What will be the effect of the Hepatitis B vaccine on the incidence of cases of the disease?

Answer: It is estimated that 40-50% of reported cases of Hepatitis B occur in male homosexuals, drug users and health care workers. With an aggressive cost-free vaccine program, the Centers for Disease Control estimates that cases could be reduced 20-30% in these high risk groups.

ALLERGY AND ASTHMA

Question: What progress has been made during the past year in research on asthma and allergic diseases? To what extent have the Asthma and Allergic Disease Centers provided new insights into the cause, treatment, or prevention of these conditions?

Answer: Two of our Centers are collaborating on studies aimed at the definitive evaluation of immunotherapy in allergic asthma caused by cat dander. Also, they are investigating a purified preparation of cat allergen for treatment purposes that will hopefully provide more protection and fewer side effects.

Three of our Centers are studying the value of applying an educational program of Self Management of Asthma, aimed at improving children's knowledge of the disease and thereby reduce morbidity and school absenteeism; early results appear promising.

Initial studies related to the clarification of the chemical structure of slow reacting substance of anaphylaxis (an important chemical mediator of inflammation that produces many of the allergic manifestations in people) have been made possible through the use of sensitive tests. These assays have enabled the measurement of these purified materials occurring only in small amounts in clinically ill individuals. It is hoped that these findings will lead to the design and development of drugs to inhibit the undesirable responses.

Another Center is in the final stages of a series of studies aimed at proving that immunotherapy with a form of poison ivy/oak extract can provide protection against this disabling form of contact dermatitis.

One Center has made significant progress in developing an animal model of occupational immunologic lung disease which will permit studies of a variety of industrial hazards that would otherwise not be possible to accomplish because of their potential hazard to humans. This is aimed at prevention of disease in the workplace and to the development of therapy.

Sensitivity tests have been developed to diagnose those at risk of developing asthma, 2-3 years before its clinical appearance. This early identification will permit certain precautionary measures to be taken in such individuals.

One Center has shown that a common food additive, metabisulfite, can be a cause of asthma in selected individuals and has developed a diagnostic approach to detection and, therefore, avoidance. The methods reported will also have relevance to the study of potential allergic effects of other food additives.

Question: Compare the proposed fiscal 1983 funding level for the Centers with previous years.

Answer: In 1981, NIAID supported 16 Asthma and Allergic Disease Centers (AADC's) for $2,758,000. In 1982, it plans to again support 16 Centers with estimated funding of $3,129,000. The 1983 budget request includes $3,487,000 for support of 16 AADC's.

Question: Can an individual "outgrow" allergies?

Answer: As there are various manifestations of allergic diseases, each one must be considered individually in order to address this question. For example, eczema can be outgrown but for the majority of sufferers persists into adulthood. Childhood asthma remits in 25% to 75% of cases. (Since numerous complications, up to and including death, can result from asthma, it should not be ignored in children in the hope it will disappear.) In general, hay fever does not begin until adolescence, worsens with midlife and improves with old age. Most food allergy is not outgrown, but the children whose food allergy was diagnosed before the age of three have a greater chance of losing their sensitivities than those whose allergies did not appear until after that age.

Question: Is there a genetic predisposition to certain allergies?

Answer: The development of allergic disease seems to result from an interplay of genetic and nongenetic (environmental) factors. There is a linkage between certain genes controlling the immune response and certain genes determining a person's tissue (HLA) type. Studies correlating tissue type with the prevalence of certain allergic sensitivities are tantalizingly suggestive of a genetic predisposition. However, the inheritance of these genes does not follow a simple inheritance pattern and much more genetic and epidemiological research needs to be done.

FOOD ALLERGY

Question: Some individuals have allergic reactions to certain foods. In addition, hyperactivity in children has been attributed to an "allergic" type reaction to food additives, although very little data have been validated and published in this area, to date. How common is food allergy?

Answer: Estimating the incidence of food allergy in the population is complicated by the absence of unequivocal objective diagnostic tests and the difficulty in differentiating truly allergic reactions from other types of adverse reactions to foods related to digestive problems. However, using available techniques, estimates of the overall incidence of food allergy vary between 1 and 3% of the population, children being more commonly affected.

Question: Are food allergy patients more often allergic to natural constituents of food, or to food additives?

Answer: True food allergies are usually associated with natural constituents of foods such as milk and peanut proteins.

Pseudo-allergic or allergic-like reactions have been attributed to food additives such as colorings, flavorings, and preservatives. Examples include the development of hives and/or wheezing after tartrazine (FD & C yellow dye #5) ingestion in aspirin-sensitive asthmatics. Metabisulfite, which is sometimes added to beverages and fresh foods, has been demonstrated to trigger wheezing, flushing and lowered blood pressure in certain chronic asthmatics.

Food additives and salicylates have been implicated in triggering the hyperactive child syndrome. This subject was addressed on January 13-15, 1982, at a Consensus Development Conference for which the NIAID was the lead sponsoring Institute. After hearing the available scientific evidence, the panel concluded that only a small portion of hyperactive children demonstrate less evidence of hyperactivity on the additive-free diets. Furthermore, the decreases in hyperactivity are often subtle and not consistently observed. The suggestion that natural constituents of food can lead to the hyperactive child syndrome has not been examined in well-designed scientific studies.

Question: What research is your Institute doing in the area of food and drug interactions?

Answer: There has been little if any evidence to indicate that food and drug interactions leading to adverse reactions or inactivation of the drug may be allergic in nature. Thus far we have not uncovered any leads for extending investigation of possible immunologic bases for these interactions; this research continues to fall within the realm of physiology, pharmacology and biochemistry.

Question: Is anything being done to educate people to the possible hazards of food interactions with the drugs they may be taking?

Answer: As we have no leads to investigate an immunologic basis for these interactions, education in this area remains in the domain of those concerned with digestion, metabolism and toxicology.

INTERFERON

Question: What is the current status of your research on interferon? Are you at all involved with the research on the possible uses of interferon in the treatment of multiple sclerosis (MS)?

Answer: At this time, the Institute is not supporting any studies in this area. An Institute representative will attend a meeting sponsored by the MS Foundation which will explore the issue of interferon treatment for MS. If funds were available and the preliminary data look encouraging enough, the Institute would be interested. At the present time clinical trials of interferon for other conditions (laryngeal papilloma), where preliminary data indicate substantial potential benefit and thus are a higher priority, cannot be funded due to budget constraints.

Question: To what extent are you supporting clinical trials of the use of this substance against viral disease?

Answer: The Institute is currently supporting two clinical studies. One is a clinical trial of interferon for treatment of initial genital herpesvirus infection in women. This double-blind trial is ongoing, and results are not yet available. Both the effect on primary infection and the frequency of recurrence will be examined. Another clinical trial is evaluating the effect of alternating cycles of interferon and adenine-arabinoside monophosphate (ara-AMP) for treatment of chronic Hepatitis B virus carriers. Ara-AMP alone is also being evaluated in this placebo controlled trial.

Question: How does your research relate to interferon research of the National Cancer Institute?

Answer: The NIAID sponsors an Interferon Information Exchange Group where representatives from the various Institutes, including the NCI, and other pertinent government agencies assemble periodically for updates on interferon research efforts. NIAID staff also serve as liaison members to the advisory group to the NCI Biological Response Modifiers Program, which monitors NCI's interferon research. The international interferon standards that are supplied by NIAID are used throughout the world for both basic research and as standards for assaying interferon in clinical trials for both infectious diseases and cancer.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

STATEMENT OF DR. RUTH L. KIRSCHSTEIN, DIRECTOR

ACCOMPANIED BY:
DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LEO H. VON EULER, DEPUTY DIRECTOR
DR. ELKE JORDAN, ASSOCIATE DIRECTOR FOR PROGRAM ACTIVITIES
WILLIAM T. FITZSIMMONS, EXECUTIVE OFFICER
GUY EARL HODGKINS, BUDGET OFFICER
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. Our next witness is another scientist long and well-known to this subcommittee, Dr. Ruth Kirschstein, Director of the National Institute of General Medical Sciences. Doctor, you direct a most important Institute. We welcome you again to our hearings. I would appreciate it if you would introduce your colleagues, and then you may give us a brief summary of your statement which will appear in total in the record, and it will give you more time to answer questions.

INTRODUCTION OF ASSOCIATES

Dr. KIRSCHSTEIN. Thank you very much.

To my left is Mr. William Fitzsimmons, the Executive Officer of the Institute, and directly behind him is Dr. Leo von Euler, the Deputy Director of the Institute.

Senator Andrews, I am honored to again present the programs of the National Institute of General Medical Sciences, the heart of which lies in elucidating the nature of life's processes at the most basic molecular and cellular levels, and in generating concepts essential to the activities supported by all the other categorical Institutes at NIH.

Exciting discoveries in basic biology are emerging so rapidly that it is fair to say that we are in the midst of that "biologic revolution" which Dr. Krause mentioned earlier. Indeed, the area of recombinant DNA technology, which Dr. Krause also mentioned, was developed, in essence, by grantees primarily from the National Institute of General Medical Sciences.

Recently, Dr. Arthur Kornberg, a long-time grantee of the National Institute of General Medical Sciences, and a Nobel Laureate, has added another milestone by learning how to "activate the switch" for the initiation of DNA synthesis in the test tube.

This work has enormous implications for understanding cell growth and possibly carcinogenesis.

Other NIGMS grantees are studying the proteins of the cell membrane which are constantly being renewed so as to assure the cell's proper functioning, particularly in the regulation of the millions of molecules that enter and leave through its membrane. And, since so many diseases are related to the malfunctioning of cell membranes, this knowledge is absolutely essential to the ultimate understanding and prevention of disease.

The NIGMS pharmacological sciences program has supported Dr. Ronald Hoffman of Cornell University, who was awarded the Nobel Prize in chemistry in 1981. His studies of certain chemical reactions are now being used by medicinal chemists to synthesize and develop new drugs.

In the area of burn and trauma research, Dr. John Burke and Dr. I. V. Yannas of Boston have developed an artificial skin for use in treating severely burned patients. This skin substitute consists of two layers, an outer layer of silicone and a bottom layer consisting of fibers of cartilage from sharks and from cowhide. This bottom layer stimulates growth of the patient's own fibrous layer. The artificial skin mimics normal skin, is not rejected as other foreign material is, and results in less scarring.

To date, Dr. Burke has successfully grafted over 40 patients with severe, third-degree burns covering 50 percent to 90 percent of their body surfaces.

But there is so much more to learn in all these exciting areas, and in order to assure and encourage the entry into biomedical research of bright young investigators, the National Institute of General Medical Sciences is preeminent in the support of research training in broad, multidisciplinary areas. This training is designed so that its graduates can serve the missions of all the other Institutes and meet the different scientific challenges of the future.

The minority access to research careers program, MARC, is a special training initiative designed to increase the number of minority biomedical research scientists. A followup of the students in the MARC honors undergraduate research training program has indicated that 85 percent go on to graduate education.

In order to continue the momentum of these exciting programs, we request a budget of $345,621,000.

I would be glad to answer any questions.

PREPARED STATEMENT

Senator ANDREWS. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. RUTH L. KIRSCHSTEIN

I am honored again this year to present to you the programs of the National Institute of General Medical Sciences (NIGMS) and to tell you of the enormous excitement that they engender. The heart of these programs is in studies which elucidate the nature of life processes at the most basic molecular and cellular levels, levels which may be fundamental to the missions of a number of the categorical institutes.

Concepts generated by grantees of NIGMS forge the tools to maintain health and ultimately will lead to the prevention of disease--cancer, diabetes, arthritis, genetic diseases and many other complex and still not understood disorders. This fundamental biomedical research, while not obviously related to any particular disease at the time it is carried out, is the essential basis for future medical studies and for preventive measures. For example, studies by NIGMS grantees on transport of sodium ions across the membranes of red blood cells have led to a way to analyze the genetics of essential hypertension in man and may have provided a clue to its cause which is currently unknown. This research, in turn, has been dependent on the concepts and techniques applicable to biological membranes and genetics, developed largely by NIGMS grantees in widely scattered laboratories.

As Dr. Paul Berg, a grantee of this Institute, pointed out in his recent Nobel Prize lecture "... dealing with disease in the future demands detailed understanding of molecular anatomy, physiology, and biochemistry ...." It is this understanding for which our grantees are striving.

Genetics

Until a very few years ago, most biologists believed that the position of genes on chromosomes was fixed, and that the same order of genes prevailed throughout all the cells of an organism. Among the most exciting discoveries in biology is what we have learned recently about DNA, the basic substance of heredity. Thought for many years to be a stable molecule, it has now been shown that segments of DNA can and do move from one part of a chromosome to another and even between chromosomes. Researchers are learning that these movable segments called transposons or "jumping genes" may play an essential role in rearranging genetic information, causing mutations and altering the way in which such information is expressed. NIGMS grantees recently have discovered the existence of previously unknown enzymes which are used to allow the movement of these "jumping genes," and many laboratories are concentrating on these exciting phenomena, trying to learn more about how genes move from one site to another and how their movements are controlled.

From these discoveries, a picture is emerging of DNA as a substance which has built into it certain adaptive mechanisms---for example, mechanisms which are responsible for tissue development and differentiation and which appear to account for the enormous diversity and variability of the proteins of the immune system.

A very recent report from the laboratory of Dr. Arthur Kornberg, a longtime NIGMS grantee and Nobel Laureate in 1959, has added another "milestone." He and his colleagues have developed, for the first time, a test tube system to "activate the switch" that turns on the duplication of DNA, starting from its origin on the chromosome. They have actually accomplished the initiation of reproduction of the chromosome of the common bacterium, Escherichia coli. Dr. Kornberg has shown that the system behaves in the test tube very much as it does in living cells. It will allow scientists to study directly the effects of drugs and other chemicals on the biochemistry of DNA replication. Such studies may have important implications for understanding cell growth and possibly carcinogenesis.

While new facts are emerging day by day in this "biological revolution," it is clear that there is much, much more to learn and that research scientists are bursting with creative ideas for expanding and applying this knowledge.

Cellular and Molecular Basis of Disease

Studies of the human cell, a tiny but very complex structure, are also blossoming at a rapid rate. We have long been aware that surface membranes play a crucial role in the functioning of cells. Among the major questions currently under study are how and where the proteins of the cell membrane are synthesized and how they are put in place. A number of NIGMS investigators, including Dr. George Palade, winner of the 1974 Nobel Prize, have evidence that proteins destined for the cell membrane enter a system of internal channels, and then make an essential stop at a unique part of the cell, the Golgi apparatus. There the newly synthesized membrane pieces are organized into the finished product and directed to the appropriate part of the membrane, in response to signals regarding the physiologic and structural needs of the cell. Thus membrane proteins are constantly renewed from within the cell assuring that the membrane of the healthy cell is always able to function properly. Since a critical feature of many diseases, such as diabetes, is a disorder of the cell membrane, it is critical to have an understanding of how the normal cell membrane is produced and functions before we can learn how malfunctions occur.

Pharmacological Sciences

The proteins on the cell membrane which are responsible for the binding of hormones and, very often, of drugs, are known as receptors. Information on the mechanism of receptor interaction with such chemicals may lead to the design of safer and more specific drugs targeted to particular cells.

An NIGMS grantee has made the surprising observation that a simple yeast has a receptor protein with a high affinity for the human steroid hormone, cortisone. This particular yeast causes a serious human infection, particularly in individuals who are being treated with cancer chemotherapeutic or immunosuppressive agents such as steroids. The binding protein found in this yeast has properties analogous to the steroid receptor of mammalian cells, an unexpected phenomenon in a unicellular organism. Further study of this receptor protein may be important in understanding why persons treated with cortisone are so susceptible to infection with this yeast.

Also of great importance are studies supported by NIGMS which are related to the structure and activity of various complex organic chemicals. In 1981, the Nobel Prize in chemistry was awarded to Dr. Roald Hoffman of Cornell University, an NIGMS grantee for a number of years. He was honored for research leading to predictions of the outcome of a certain class of chemical reactions. Many of these reactions are being used by medicinal chemists to develop new drugs and other synthetic materials necessary to combat disease.

Physiology and Bioengineering

Infection is a great danger in persons suffering from severe burns, and covering the burned surfaces as soon as possible can prevent such debilitating infections. During the past year Dr. I.V. Yannas of Massachusetts Institute of Technology and Dr. John Burke of Harvard University, supported by NIGMS, have reported an important development in producing an artificial skin for use in immediate closure of extensive burn wounds. This skin substitute, like human skin, has two layers, the top one made of silicone. The fibers of the bottom layer, consisting of a mixture of proteins from cowhide and shark cartilage, stimulate the growth of the patient's own fibrous layer and eventually are replaced by it. Twenty-seven days after it is put in place, the temporary outer silicone layer is removed and replaced by small pieces of superficial tissue removed from the remaining normal skin of the patient.

Dr. Burke has recently reported on successful grafting of this artificial skin in 40 patients having third-degree burns covering 50 percent to 90 percent of their bodies. In the follow-up period, the wounds that had been closed by artificial skin showed less scarring than is usually seen after conventional skin grafts.

Despite this encouraging advance in the surgical treatment of burn patients, much remains to be learned about the cascade of organ, tissue, cellular and molecular changes that follow severe burns and trauma. Further improvements are needed, necessitating basic studies of the profound biochemical systemic changes that occur at the cellular and molecular level.

Research Training

As in years past, the National Institute of General Medical Sciences continues to be the preeminent Institute at the National Institutes of Health in regard to the support of research training. Based on the conviction that a flourishing scientific community is vitally dependent on the continuing entry of bright new investigators with fresh points of view, the NIGMS feels that it is critically important to offer training grant and fellowship support in the biomedical sciences. These awards offer encouragement and strengthen the motivation of young individuals about to enter scientific careers, by showing a long-term commitment of the Nation to a healthy biomedical research enterprise. The awards are also important in setting high standards for multidisciplinary scientific training that will give the graduates the versatility to meet a broad range of scientific challenges. In this way they can expect to be active in the laboratory for long periods of time.

Minority Access to Research Careers (MARC)

The unique research training initiative, Minority Access to Research Careers (MARC), is designed to increase the number of minority scientists engaged in biomedical research and to strengthen the research and training capabilities of minority institutions. In order to increase further the scientific career opportunities for graduates of the MARC Honors Undergraduate Program through graduate training at major research universities, the Institute initiated a special individual predoctoral fellowship program in 1981, and four awards were made last year. This logical extension of the Honors Program to graduate education builds on the contacts that trainees in the undergraduate programs have made during summers or semesters spent at major research institutions throughout the country. This latter feature is an important and unusual aspect of the Honors program.

A continuing followup of students who have received support under the MARC Honors Undergraduate Research Training Program has shown that some 85 percent of these young men and women have continued their education beyond college. Moreover, their success in these advanced studies has made them excellent "role models" and has resulted in a substantial increase in the number of science majors at these minority institutions.

Mr. Chairman, to support the research and research training programs I have outlined and to sustain the momentum of the basic scientific advances in biology now being made, the budget request for the National Institute of General Medical Sciences for Fiscal Year 1983 is $345,621,000. I shall be pleased to answer any questions and to supply any additional information desired.

BIOGRAPHICAL SKETCH

RUTH L. KIRSCHSTEIN, M.D.

POSITION:	Director, National Institute of General Medical Sciences
BIRTHPLACE and DATE:	Brooklyn, New York October 12, 1926
EDUCATION:	A.B., magna cum laude, Long Island University, 1947 M.D., Tulane University School of Medicine, 1951
EXPERIENCE:	Director, National Institute of General Medical Sciences, September 1974-present Deputy Associate Commissioner for Science, FDA, 1973-1974 Acting Deputy Director, Bureau of Biologics, FDA, 1972-1973 Assistant Director, Division of Biologics Standards, NIH, 1971-1972 Chief, Laboratory of Pathology, DBS, NIH, 1965-1972 Acting Chief, Laboratory of Pathology, DBS, NIH, 1964-1965 Assistant Chief, Laboratory of Viral Immunology and Chief, Section of Pathology, DBS, NIH, 1962-1964 Chief, Section of Pathology, Laboratory of Viral Immunology, DBS, NIH, 1960-1962 Medical Officer, Pathologist, Laboratory of Viral Products, DBS, NIH, 1957-1960 Medical Officer, Resident in Pathology, Clinical Pathology, Clinical Center, NIH, 1956-1957 Trainee of National Heart Institute and Instructor in Pathology, Tulane University School of Medicine, 1954-1955 Resident, Pathology, Providence Hospital, Detroit, Mich., 1952-1954 Assistant Resident, Pathology, Veterans Administration Hospital, Chamblee, Ga., 1952 Internship, Medicine and Surgery, Kings County Hospital, Brooklyn, N.Y., 1951-1952
ASSOCIATION MEMBERSHIPS:	American Association of Immunologists American Association of Pathologists American Society of Microbiology
SPECIAL AWARDS or CITATIONS:	DHEW Superior Service Award, 1971 PHS Superior Service Award, 1978 Presidential Meritorious Executive Rank Award, 1980
COMMITTEE MEMBERSHIPS:	Invited member of World Health Organization Expert Group on International Requirements for Biological Substances, Geneva, Switzerland, 1965 and 1971 Invited consultant to World Health Organization concerning problems related to the use of Poliovirus Vaccine, Live, Oral. Geneva, Switzerland, 1967 Member, Board of Consultants, Journal of Medical Pathology Member, Primate Research Centers Advisory Committee, Division of Research Resources, NIH, 1971-1975 Member, National Commission on Diabetes, 1975 Member, National Commission on Arthritis and Related Musculoskeletal Diseases, 1975 Member, *Ad Hoc* Committee on Reserpine and Breast Cancer, 1974-1977 Chairperson, NIH Grants Peer Review Study Team, 1975-1976 Member, Editorial Board, Journal of Toxicology and Environmental Health Member, Scholars-in-Residence Advisory Committee, 1977-present Member, NIH Coordinating Committee on Manpower, 1978-present

RESEARCH AND TRAINING COST CONTROLS

Senator ANDREWS. Thank you, Doctor, for summarizing your initial statement. The overall budget proposes to cap indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent, and to maintain training allowances slightly below the fiscal 1982 level.

What will these policies mean to your research and training efforts, and what will they do to the availability of grant recipients to produce good science and good research, as I have asked your other colleagues who have appeared here this morning?

Dr. KIRSCHSTEIN. Senator Andrews, as a result of these policies, some difficult choices will have to be made. Since all of the Institute's programs are very exciting, we will try to maintain a balance between them. Of necessity, there will have to be a slowdown in the progress that can be made on individual research projects in all of the exciting areas of research that I have mentioned.

Although promising research ideas are burgeoning, the grantees will have to perform somewhat fewer experiments. There will be slowing of progress.

CONTINUING RESOLUTION IMPACT

Senator ANDREWS. Doctor, what has been the impact of the continuing resolution which imposed the lower of the House and Senate figures, and a reduction of 4 percent beyond that?

Dr. KIRSCHSTEIN. Senator Andrews, the continuing resolution has had an impact in that there will be fewer research grants and fewer trainees supported. Each research project grant will be reduced by approximately 3 percent. The National Institute of General Medical Sciences allocates about 80 percent of its funds for the support of individual investigator-initiated research grants. These represent the lifeblood of the programs that we support. The fiscal year 1982 continuing resolution provides nearly $11 million less for such grants than did the Senate allowance.

IN-HOUSE TRAINING EFFORTS

Senator ANDREWS. You mentioned in your opening statement, of course, that you are the Mother Superior of all of these new researchers that come up, that this is the most important Institute, and then you are concerned about reducing the grants out in the field.

Are you making a special effort in-house to keep the inflow of these bright potential researchers coming into your shop?

Dr. KIRSCHSTEIN. Senator Andrews, the National Institute of General Medical Sciences does not have the usual type of in-house, laboratory-based, or intramural program that the other Institutes have. We do have one small, unique intramural program, the pharmacology research associate training program—PRAT—which supports 22 bright young investigators in postdoctoral fellowships in some of the outstanding intramural laboratories of the other Institutes at NIH.

For example, preceptors for this program include Dr. Julius Axelrod and Dr. Marshall Nirenberg of the NIH intramural program, both of whom are Nobel Laureates. We will maintain the PRAT program at its current level. The PRAT fellows represent a cadre of highly trained scientists who will pursue research in pharmacology in the future.

The NIGMS extramural program of support for research training is designed to assure the maintenance of an adequate national pool of bright, young researchers for the future.

INDIRECT COSTS AND TRAINEE EXPENSES

Senator ANDREWS. The committee, of course, has looked at the amounts that are budgeted for the institutional allowances and the indirect costs for training these researchers. In these areas your particular shop was, in 1981, at the $16 million level. The nearest rival has been the Heart Institute at $9 million; Cancer goes down to $7 million; Neurology is only $2.6 million; Allergy is $2.6 million; and Eye way down at $1.2 million.

So you are really the big factor in that. But you've gone from $16.2 to $10.3 million in the 1982 estimate, and now down to the $9.8 million in the 1983 estimate.

Does this decrease concern you in light of the material you have included in your opening statement?

Dr. KIRSCHSTEIN. Senator, the NIGMS is, as you stated, the preeminent Institute in research training. We support over two-thirds of all the predoctoral training supported by NIH at universities and medical schools throughout the country. And, indeed, we support about one-third of all the research training funded by NIH.

With the reduction in the trainee-related expenses, usually called institutional allowances, institutions which provide research training will be unable to support at least some of the activities that are associated with the highest quality training.

For example, trainee-related expenses are used to support seminar speakers, so that trainees can learn from outstanding researchers affiliated with other institutions; to provide supplies for studies in which trainees engage as they learn how to do research; to provide funds for trainees to attend scientific meetings, where they again will learn from other scientists the theories, techniques, and activities developing in their field of research.

This will probably have some impact on research training. However, the budget constraints with which we all must live require some degree of cutbacks.

PRIVATE SECTOR FUNDING

Senator ANDREWS. Well, Doctor, the concept that is being put forward by this administration is that the private sector is willing, able, and eager to step in and take over.

I don't necessarily agree with all the points the administration is making in this and other fields, but I'd appreciate your evaluation of what you see taking place.

Is the private sector taking over some of this work that you have been doing? Is there a stimulus coming to provide the support for these seminars and the other things you have just described to the committee?

Dr. KIRSCHSTEIN. Senator, as Dr. George Keyworth, the President's Science Advisor, recently has stated, it is most appropriate for the Federal Government to be the primary supporter of basic research. The private sector's support in general occurs after the foundation of basic research developments has been laid, as this knowledge begins to be applied into the development of both new products and new technologies. Therefore, it is our feeling that the kind of basic research and research training support, which our Institute provides, has to come from Federal funds.

Senator ANDREWS. But what you're telling the subcommittee, then, Doctor, and the readers of the record, is that the private sector is not stepping in to pick up the slack created by the cutbacks that are manifested in your budget for this type of training.

Dr. KIRSCHSTEIN. I think, as was stated by the President's Science Advisor, the Federal Government does not expect the private sector to replace it in the area of basic research.

Senator ANDREWS. The point still remains—and you've gone around end quite well [laughter]—that there isn't anybody doing this right now in the area that you have cut back from. Is that essentially correct?

Dr. KIRSCHSTEIN. We will try to maintain our support of high-quality research and research training to the best of our ability, Senator.

Senator ANDREWS. Well, the point is you are not maintaining that area. As I pointed out to you, you've been cut from $16 to $9.8 million, a cut of about 50 percent, in 2 years. And the question that I was trying to develop is: Is the private sector moving in to pick up this most important field? And I can define from the conversation you just supplied me with that, no, they're not.

Dr. KIRSCHSTEIN. That's correct. Although the private sector funds some research and research training, the effort is generally limited and in more applied fields.

Senator ANDREWS. And there is no other source?

Dr. KIRSCHSTEIN. It is unlikely that there are other funding sources for the type of research and training which NIGMS provides.

Senator ANDREWS. And it isn't the type of research you anticipate or the President's Science Advisor anticipates down the line, that private industry will step in and support.

Dr. KIRSCHSTEIN. That's correct.

EFFECTS OF BUDGET CUTS

Senator ANDREWS. And if that doesn't happen, then what?

What happens down the line if you cut this program in half?

You are also cutting or being asked to cut capitation grants for medical schools because they say there are plenty of doctors around. I have a lot of counties that don't have a single general practitioner, and I take a dim view of some of that. But when we cut all this, what's coming in to substitute for it?

Do you have any idea what's going to happen 5 years from now if we continue these cuts?

Dr. KIRSCHSTEIN. Since research training is, just as you indicated, Senator Andrews, long range, and since the trainees that we are supporting today will only become researchers about 10 years from now, as fewer trainees are supported and provisions for high-quality, structured training programs are reduced, there may be some difficulties in the future.

Senator ANDREWS. I remember an old friend and colleague of mine by the name of John Fogarty, who now has his name on your Institute, and John, of course, always used to say, and said quite well, that if you don't have the researchers around, you're not going to get the end results, and there is no substitute for it.

Have you found a substitute in the last couple or 3 years?

Dr. KIRSCHSTEIN. No, sir.

Senator ANDREWS. No substitute?

Dr. KIRSCHSTEIN. No.

DR. KORNBERG'S RESEARCH

Senator ANDREWS. Finally, Doctor, in order to maybe highlight the importance of research, could you speak to the significance of the work of Dr. Arthur Kornberg out at Stanford who apparently has developed a method of DNA replication outside the cells?

Dr. KIRSCHSTEIN. Yes, sir; I mentioned Dr. Kornberg's work briefly in my opening statement.

Senator ANDREWS. That's right, and I was intrigued by it. and I thought perhaps by spending a moment or two on it we might give a concrete example of how important research is.

Dr. KIRSCHSTEIN. Dr. Kornberg has been working in this area of DNA synthesis for many, many years. Indeed, he started his research career as an intramural scientist at NIH and left, moving first to Washington University at St. Louis and then to Stanford University where he has been, as I said, studying DNA synthesis for many years.

When he made the announcement of his recent discovery, he noted that the mechanism for initiating DNA synthesis, had eluded him for many years, and that it was only recently, partly through the availability of recombinant DNA technology, that he was able to finally find the way to do this.

What has actually happened is that Dr. Kornberg and his colleagues have been able to initiate or activate the "switch," for the reproduction of the chromosome of the common bacterium, Escherichia coli, in the test tube. Dr. Kornberg has shown that this system behaves in the test tube almost exactly as it does in the bacterium itself. His discovery will now allow scientists to study outside living cells, in a more controlled experimental environment, the effects of drugs and other chemicals on the biochemistry of DNA replication. This also has enormous implications for understanding cell growth, for investgating the induction of malignancy, and the impact of chemicals—sometimes carcinogenic chemicals—on the human organism.

Dr. Kornberg and his colleagues are continuing this work under the support of NIGMS. We are pleased to have supported Dr. Kornberg for many, many years, and to have funded two of the researchers working with him on these experiments by means of a predoctoral research training grant at Stanford University.

Senator ANDREWS. Doctor, how much time did Dr. Kornberg spend at NIH as a young scientist, developing scientist, do you know?

Dr. KIRSCHSTEIN. I believe it was 10 years.

Senator ANDREWS. In other words, we might say that part of the discipline and part of the scientific knowledge of this individual wouldn't be there if it hadn't been for the training ground that he found at NIH.

Dr. KIRSCHSTEIN. Absolutely.

Senator ANDREWS. He is then, as a Nobel Prize winner and all the rest, a product of the system that we have been talking about for the last few minutes that now is being cut back.

Dr. KIRSCHSTEIN. That is absolutely true, sir.

SUBMITTED QUESTIONS

Senator ANDREWS. Thank you, Doctor. We have some other questions which we will include for the record, and if you can provide those answers at the time you provide the corrected hearing transcript, we'd appreciate it.

Dr. KIRSCHSTEIN. Thank you, sir.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: In FY 1983, expenditures for direct operations and program management will account for only 3% of the Institute's budget, or about $11 million. Salaries and benefits for Institute staff account for almost half of this amount, or approximately $5.1 million. But, current staffing levels are substantially below those of 10 years ago when fewer grants were funded; and the Institute feels that its personnel-related expenditures represent the minimum necessary to prudently administer the approximately 3,000 grants funded by NIGMS. In addition, the Institute has little control over the determination of costs for centrally furnished services (roughly $3.8 million in FY 1983) or the amount allocated for Departmentally sponsored program evaluation projects (roughly $1.1 million). The Institute will continue, however, to hold controllable administrative costs to a minimum; and, as in past years, only requests for essential travel, communications, supplies, and equipment will be approved.

Question: What are your most important administrative concerns and what are your least important concerns?

Answer: Because NIGMS has only a very small program of intramural research on the NIH campus, the Institute's administrative concerns primarily relate to the need for the resources necessary to properly administer its grant programs. Sufficient numbers of skilled scientific and support staff are increasingly difficult to sustain, for example. Also, it is essential to perform an adequate number of site visits to evaluate the scientific merit and progress of research projects and to keep the Institute's scientist administrators up-to-date in their knowledge of the areas of science relevant to the Institute.

The Institute's least important administrative concern is hard to name, but is probably space. The Institute's staff are adequately housed in rental office space in Bethesda, Maryland.

Question: What criteria do you use for determining your administrative priorities?

Answer: Maintaining a high quality staff having wide knowledge and understanding of relevant biomedical research fields is the Institute's first administrative priority. Beyond that, before approving controllable administrative expenses the Institute evaluates the extent to which the proposed expenditures contribute directly to the Institute's prudent and efficient stewardship of its grant awards. Only the most critical goods and services are procured.

FRAUD AND ABUSE

Question: Congress has recently been investigating charges of fraud and abuse of research contracts and grant funds in other Institutes at NIH. Have you had any problems along this line?

Answer: To date, the National Institute of General Medical Sciences has not had any problems with fraud and abuse involving research contract and grant funds.

Question: What are your mechanisms for detecting fraud and abuse?

Answer: Our primary mechanism for detecting fraud and abuse is basically to have a very well-trained, conscientious and vigilant staff. All applications for competing or noncompeting grants are scrutinized by grants management and program staff to be sure that both fiscal and scientific contents are in order. If any unusual or unexplained facts are noted, Institute staff follows up with a telephone call or letter to the principal investigator or the business office of the institution. Any discrepancies or errors are immediately corrected. If any significant changes in scientific direction or budget have taken place, an explanation or justification is sought.

Question: How effective have those mechanisms been for preventing fraud and abuse?

Answer: We feel our procedures have so far been able to detect potential problems at an early stage and to correct them. The institutional officials and the investigators have cooperated with us by notifying us of any discrepancies of which they have become aware and by responding to our requests for clarification or correction.

Question: What actions are taken against individual researchers or research hospitals not following your directives?

Answer: Fortunately, we have not had to take action against individual researchers or research institutions for not following our directives. Should such cases occur, they would be referred to the Office of the Director, NIH for action. This office is preparing formal procedures for handling possible fraud and abuse situations.

PROGRESS IN CATEGORICAL AREAS

Question: Please bring us briefly up-to-date on your progress in the areas of --

-- Cellular and Molecular Basis of Disease
-- Genetics
-- Pharmacology
-- and Biomedical Engineering

Answer:

Cellular and Molecular Basis of Disease

Recent research advances funded by the Cellular and Molecular Basis of Disease Program have occurred over the broad spectrum of studies on the cell and its components. Among the most notable areas of progress in research on the cell and its components are those surrounding the structure and activity of enzymatic proteins critical to cellular function. Exciting work is underway both in physical studies of protein structure and in biochemical aspects of their enzymatic function.

Several studies of a theoretical and mathematical nature are focusing on the forces between atoms in proteins. Using very sophisticated computer technology, a number of investigators including Dr. Barry Honig at Columbia University and Dr. Francis Salemme at the University of Arizona are examining the interactions between the various atoms in proteins and the ways these interactions determine the folding and stable three-dimensional configuration of these complex molecules. In addition, Dr. Stuart Rice at the University of Chicago has been using these techniques to study the role played by water molecules in the folding of proteins and in the interactions between proteins. The results of these studies have led to major advances in the understanding of several critical interactions, such as between antigens and antibodies, between drugs and their cellular receptors, and between proteins and their nonprotein components.

Nonprotein components are critical elements in enzymatic function, and metals have long been known to be among these components. However, the details of how these metals are held and positioned in proteins have proven elusive, thus preventing a complete understanding of the mechanism of enzyme function. An enzyme named cytochrome oxidase, a part of the pathway responsible for turning foodstuffs into energy, is known to contain iron and copper, but their arrangement has been unclear. Dr. Britton Chance and his collaborators at the University of Pennsylvania have used a sophisticated instrument, a synchrotron, to determine the structure of the protein in the neighborhood of these metals. They have found that the iron and copper are linked together by a sulfur bridge, a surprising result and one that contributes to our growing understanding of the role of sulfur in the cell's production of energy and other cellular functions.

Another aspect of the study of protein structure that has advanced recently is the ability to determine the amino acid sequence of extremely small amounts of protein. Certain types of proteins have proven to be very difficult to purify and to isolate, yet knowledge of the sequence and structure of these proteins is critical. To deal with this problem, a grantee at the California Institute of Technology, Dr. Leroy Hood, has developed an entirely new method of protein sequencing that is much more sensitive. It is now possible to determine the amino acid sequences of key cellular proteins found in only trace amounts. This technology is being improved further, and it promises a vast increase in the number of proteins whose sequence is known.

For proteins that are very difficult to sequence, another technology is being developed and utilized by many NIGMS grantees. If an amino acid sequence at the end of such a protein can be determined, the rest of the protein sequence can be found using recombinant DNA technology to isolate the gene for this protein. Using this method, not only can the protein sequence be determined from the gene sequence, but the protein can also be synthesized in test tubes. The power of these combined techniques cannot be overemphasized. It will now be possible to synthesize in test tubes many rare proteins, perhaps found only in genetic diseases, facilitating detailed studies of the nature of the genetic defects.

Recombinant DNA technology has been used in another way to study the interaction of two forms of an important cellular protein, tubulin. Tubulin is the basic component of microtubules, cellular structures which determine cell shape, movement, and division. Microtubules are known to be composed of two forms of tubulin, but the mechanism by which tubulin is assembled into microtubules is not fully understood. Two NIGMS grantees, Drs. Don Cleveland and Marc Kirschner of the University of California have used recombinant DNA technology to isolate the genes for tubulin. They have found that there are separate "families" of genes which code for the two types of tubulin and that these "families" of genes are on different chromosomes, a rather unusual situation for functionally related genes. Drs. Cleveland and Kirschner have determined the amino acid sequence of the tubulins, and they are now in the exciting position to answer critical questions about microtubule structure.

An important aspect of protein structure is the extent to which it can be modified by enzymes. Such modifications seem to regulate some enzyme activity. One modification, enzyme phosphorylation, may occur in a wide variety of cellular activities. Dr. Glenn Kuehn at the New Mexico State University has been successful in revealing an elegant regulatory sequence involving an enzyme called ornithine decarboxylase (ODC). Because all cells begin to produce ODC when they are stimulated to grow and divide, this enzyme is especially important. Dr. Kuehn has shown that this enzyme is controlled by another enzyme whose sole function is to add phosphate groups to ODC, thereby inactivating it. This phosphorylating enzyme is, in turn, controlled by the product of ODC itself. Thus, a very finely balanced regulatory sequence of several proteins involved in cell proliferation exists. Furthermore, it now appears that interferon, known for its inhibition of cell growth and division can induce the synthesis of the phosphorylating enzyme which inactivates ODC. It is possible that this may be a key action of interferon.

Many of the advances in cellular and molecular research employ highly analytical procedures requiring instrumentation at the frontiers of research technology. Improvements in various types of resonance and fluorescence spectroscopy, in neutron and electron diffraction, in computer analysis and modeling are emerging as a result of the demands of these cellular and molecular studies. The use of the synchrotron in studies described above was pioneered specifically because of the need to make finer measurements of protein structure. This technology, like others developed on research projects supported in this program, will be extended and applied to a wide range of research and some may possibly be used in medical practice.

Knowledge of the structure of proteins and of its contribution to proteins' enzymatic activities is essential to the integrated understanding of cellular functions. Because they compose the functional machinery and structural materials of the cellular components, proteins are responsible for the ongoing work and life of the cell. While these advances portray some of the excitement and progress now occurring in cellular and molecular biology, significant accomplishments are also taking place in many other areas of this program.

Genetics

Recent advances in genetics have revolutionized our views of how genetic material is organized and expressed. Only a decade ago, DNA was thought of as a stable, highly conserved molecule and chromosomes as linear arrangements of genes, each of which carried the information for the manufacture of a single protein. The analogy was an "encyclopedia" of an individual's total genetic composition, in which the information was arranged in a fixed order and into which "typos" or mutations were occasionally introduced. The emerging view depicts DNA as a dynamic molecule, continually altered by physical, chemical, and biological insults from the environment, and actively reedited and reorganized by enzymes in a valiant and usually successful effort to preserve the original message.

This new view has emerged largely through use of recombinant DNA technology, which was pioneered by several grantees of the National Institute of General Medical Sciences (NIGMS). This technology involves snipping specific genes or regions of DNA from the chromosome and inserting them into carrier molecules (called plasmids) so that they are readily available for detailed study. These approaches have had profound effects on genetics research, ranging from basic, molecular studies to studies concerned with the transmission of diseases in human populations. Thus, recombinant DNA technology has become a tool which enables scientists to test concepts which would have been virtually impossible to examine a few years ago.

An excellent example of such a concept is the transposable element. In the past, these elements, called "jumping genes," were very difficult to study and were felt to be exceptions to the general rule of DNA stability. With the recent use of recombinant DNA, transposable elements have been found in nearly every organism that has been studied and appear to be very important. Scientists have shown that when genes move to new positions, their expression and that of nearby genes may be altered much as a sentence in a book, when transposed to a new location and read in a new context, may lose its original meaning or take on a new one. Transposable elements may account for the enormous diversity and variability of the proteins of the immune system.

Recombinant DNA technology has also helped scientists study how genes are organized on chromosomes. Genes which are structurally and functionally related are often found clustered together on chromosomes. Such gene clusters or families are characteristic of genes for hemoglobin and for some other important proteins. Occasionally, single genes from such clusters are found at some distance from their families. These genes, called orphons, have only recently been found, and their importance to gene expression is still unclear. However, their existence has contributed to the view of DNA as a dynamic molecular system.

Another important application of recombinant DNA technology has been in mapping human genes. In the past, gene mapping in plants and animals was done by studying hundreds of offspring of carefully characterized parents. Clearly, such studies are impossible in humans. Geneticists have recently developed procedures for locating human genes by using recombinant DNA and cell culture technologies. To date, over 400 genes have been mapped to precise locations on human chromosomes.

Recombinant DNA technology is also contributing to an explosion of research activity in the field of developmental genetics. One of the most intriguing biological problems concerns the mechanisms whereby undifferentiated embryonic cells are progressively altered in structure and function to form the highly specialized cells (e.g. bone, muscle, nerve and blood cells) comprising the developed organism. Since every cell of that organism contains the same complement of genes, it is clear that complex patterns of gene regulation must control the successive stages in development. Genes must be turned on and turned off at the appropriate time and place. Some of the burgeoning research in this area uses Drosophila, a fruit fly. A large number of genes contribute to normal and abnormal developmental changes in Drosophila and are under active investigation.

Other recent advances in genetics research include the discoveries of a reversed DNA helix structure, of the modification of DNA by addition of methyl groups, and of the exact transmission of the mother's mitochondrial DNA to her offspring. These discoveries have suggested a host of new approaches to the study of the genetics of man and his diseases.

These advances are but a small part of an explosion of information in genetics. Discoveries and refinements of genetic models are occurring at an unprecedented rate, and our understanding of basic molecular processes, gene expression, chromosome organization, DNA replication, development and differentiation, and evolution is considerably more refined now than even a year ago. The promise of new, useful information is both tantalizing and exciting.

Pharmacology

A number of significant research findings have come out of the NIGMS Pharmacological Sciences Program over the past year. These include the following:

1. Previously, NIGMS reported the discovery of prostaglandin D_2 in humans by Dr. John Oates of Vanderbilt University and his collaborators. Among their many functions, the prostaglandins (and specifically PGD_2) which are formed in the mast cells along with histamine, have now been shown to mediate certain hypersensitivity reactions. Systemic mastocytosis, an abnormal proliferation of mast cells with serious, occasionally fatal symptoms, has now been characterized biochemically. Patients with this disease can be accurately identified and controlled with combinations of antihistamines and aspirin. With the availability of specific biochemical diagnostic criteria, this disease, once thought to be extremely rare, has now been shown to be relatively common. In the future, afflicted individuals will be able to find relief from the flushing and occasionally severe hypotension which this disease causes.

2. Enzymes are proteins which serve as catalysts in the millions of chemical reactions taking place in the body. With the aid of enzymes, the cells of the body carry out the complicated synthesis of biologically critical molecules such as hormones and vitamins. However, when chemists attempt to synthesize these molecules in the laboratory, many laborious and expensive steps are required, producing mixtures of active and inactive forms of the molecules in only low yields. Recently, however, Dr. George Whitesides, an NIGMS grantee from MIT, has developed an approach in which he has been able to trap and stabilize isolated, purified enzyme proteins in a form in which they can be used to catalyze chemical transformations in the test tube. Using these immobilized enzyme systems, Dr. Whitesides is now making possible the development of new routes to synthesize complicated molecules of biological and therapeutic importance which, until now, had to be expensively isolated from animal sources.

3. Studies on the mechanisms of toxicity of various drugs can provide information to improve the safety of drugs; but, just as

important, they can lead to an understanding of basic biological mechanisms. The aminoglycoside antibiotics, such as gentimicin, are currently the most frequently used drugs in cases of infection with gram negative organisms. However, these drugs sometimes produce kidney damage in patients being tested. With this in mind, Dr. Paul Lietman of Johns Hopkins University has been studying the way in which gentimicin binds to kidney cell receptors, and enters the cells of the kidneys. He has found that gentimicin is taken up by the cells of the renal tubule brush border, and that this uptake is not the same as that used by the renal brush border for extracting sugars and amino acids. Furthermore, Dr. Lietman has discovered that naturally occurring polyamines, such as spermine, can inhibit and reverse the transport of this antibiotic. These results are of particular interest since the biological roles of the polyamines are not fully understood. In addition to providing ideas for the synthesis of safer, less toxic antibiotic molecules, Dr. Lietman's work is now providing information on kidney cell receptors and the role of the polyamines.

Other grantees supported by the Pharmacological Sciences Program are combining the experimental approaches of chemistry, molecular biology, and genetics with those of pharmacology to advance our knowledge of the relationship of receptor function to disease and to therapy.

Biomedical Engineering

NIGMS grantees in the field of Biomedical Engineering are reporting good progress in the development of instrumentation with increased capabilities for quick, accurate measurements of exceedingly small amounts of biologically important substances. Other workers are extending the capability to represent extremely delicate features of biologic structure in three dimensions. This technology is primarily designed for the experimental laboratory, and is allowing investigators working at the cellular and molecular levels to make ever more basic and detailed observations. Some examples of notable progress follow:

1. Drs. Christie Enke of Michigan State University and Fred McLafferty of Cornell University, working independently, have significantly extended the utility of the mass spectrometer by developing special combinations of mass spectrometric instruments that permit analysis of heavier, more complex compounds, such as protein hormones, as well as certain drugs and their metabolites.

2. Incorporating several advanced techniques, a cell sorter developed by Dr. Leonard Herzenberg of Stanford University is finding application in a growing number of biologic investigations. It has been shown, for example, that the hybridoma technique for producing pure antibodies is materially aided by the ability of this cell sorter to separate live single cells with specific immune characteristics.

3. The resolution of biologic features possible with electron microscopes has been amplified with the aid of computers; and this combination of computers and scientific instruments is being used increasingly to study complex molecules, as well as

cellular structures. Dr. Wah Chiu of the University of Arizona, for example, has been determining the structure of large peptides at a level of resolution that will almost distinguish individual atoms--a major advance in instrumentation capacity. The peptides being studied by Dr. Chiu are especially interesting in that their three dimensional structure is such as to allow them to be inserted into the double helix of DNA and then to destabilize the helix. This process appears to be critical to DNA replication and genetic recombination in the virus which has been used for these studies.

In addition, promising developments are taking place in the construction of devices for the continuous monitoring of physiologic functions and in the refinement of techniques for separating and isolating biologically important substances.

ARTIFICIAL SKIN

Question: We gather researchers funded by your Institute have developed an artificial skin useful for closing extensive burn wounds. How successful is this development -- and when will the skin be available for general use?

Answer: Investigators funded by the National Institute of General Medical Sciences (Dr. I. V. Yannas of M.I.T., and Dr. John Burke of Harvard University) have developed an artificial skin for use in the closure of severe and extensive burn wounds. This skin substitute, like human skin, has two layers. The top one is made of silicone. The fibers of the bottom layer, consisting of a mixture of proteins from cowhide and shark cartilage, stimulate the growth of the patient's own fibrous layer and eventually are replaced by it. This artificial skin is now being made in the laboratory of Dr. Yannas and stored for use in operating rooms at the Massachusetts General Hospital. Dr. Burke has performed successful grafts of this skin substitute on more than forty patients having third-degree burns which cover 50 to 90 percent of their bodies. At the present time, when the outer temporary silicone layer of this artificial skin is removed after twenty-seven days, it is replaced by small pieces of superficial tissue from the remaining normal skin of the patient. The skin graft grows and forms a permanent cover of the wound. This method has prevented infection in burn wounds, which, on follow-up, show less scarring than is usually seen after the use of conventional skin grafts.

A pharmaceutical company in Kansas is currently developing the capability to manufacture this artificial skin and anticipates that it will be available for general use in about two years.

It should be noted that Dr. Yannas is continuing to develop new and improved methodology by pursuing additional studies. When the artificial skin is placed over a burned area, Dr. Yannas now adds dispersed cells from normal skin to the bottom layer. The outer silicone layer is then placed on top as protection. In his initial findings, Dr. Yannas has noted that when the artificial skin is removed after two to three weeks, the wound has been closed by mature, confluent, multilayered skin which has grown from the seeded cells. Indeed, there seems to be no need for further grafting. Dr. Yannas feels that only a tiny piece of normal skin will provide enough cells to cover the entire wound.

MARC PROGRAM

Question: What accounts for your plan to increase funding for the Minority Access to Research Careers (MARC) Program by $633,000 in Fiscal 1983?

Answer: The proposed increase in the budget for the MARC Program is designed to allow two things: (1) a modest increase of 20 in the number of individuals receiving support for research training under this program, and (2) an increase in the average cost of supporting each trainee. This is related to increases in tuition, stipends, indirect costs, and trainee-related expenses (institutional allowances).

Question: To what extent is the Honors Undergraduate Research Training Program being emphasized over the other activities supported under MARC?

Answer: Over 80% of the MARC Program budget has been allocated to the Honors Undergraduate Program. This reflects a recognition on the part of the Institute that the best way to accomplish the major objective of the MARC Program--increasing the pool of minority biomedical scientists who are effectively competing for NIH research grants--is to provide research training opportunities at the undergraduate level which will assist minority students in gaining entry to the nation's best predoctoral programs in the biological sciences. The success of this program to date--85% of its graduates have gone on to some form of advanced study in the biomedical sciences--is very encouraging; and this too has been a factor in the formulation of the Institute's 1983 budgetary decisions in this area.

Question: Contrary to NIH-wide policy in Fiscal 1983, you propose to pay full institutional allowances and indirect costs under the Undergraduate program. What is the reason for this?

Answer: Among the major problems faced by the institutions supported by the MARC Program is the lack of adequate resources and facilities of the kind needed to provide truly high quality teaching and research training experiences for the students. These schools lack the funds to hire needed new faculty, to purchase up-to-date equipment, and to provide necessary laboratory supplies for their students. As a result, institutional allowances and indirect costs play an even more critical role in relation to the research training activities supported by the MARC Program than is the case with other NIH supported research training activities. With this in mind, a decision was made to obtain a special exception for the MARC Program.

Question: To what extent are the MARC and Minority Biomedical Support (MBS) programs duplicative or complementary--and is there coordination between the two?

Answer: The MARC and MBS programs have different purposes and are complementary. The MARC Program focuses on research training activities, aimed at increasing the number of minority students entering biomedical research careers. The MBS Program, by contrast, is geared to the support of research projects and institutions. The MBS, soon to be renamed the "Minority Biomedical Research Support Program" (MBRS) does not support research training per se. Coordination between the MARC and MBS programs is achieved through both formal and informal communication between the staffs of the two programs.

POLYGENIC DISEASES

Question: What progress has been made in understanding the causes of the so-called polygenic diseases, which include hypertension, atherosclerosis, diabetes, cancer, and schizophrenia?

Answer: The causes of many common diseases, such as heart disease and schizophrenia, are complex. They are "genetic" diseases in the sense that they tend to run in families; but progress in understanding the genetics of these diseases has been slower to develop than in the case of diseases with simpler genetic relationships, such as sickle cell disease or Tay-Sachs disease. Common diseases are inherently more difficult to study. Each of them, cancer or heart disease for example, actually represents a complex of many different diseases, probably with many different causes; and their course is influenced not only by genetic factors, but by environmental variables such as diet, smoking, and stress as well. Overt expression of the diseases often occurs in middle age or later; thus, it is often not apparent which of an affected individual's children carries the disease, and which genes are involved.

Nevertheless, there has been steady progress in our understanding of these diseases. Some years ago, for example, studies of the survivors of heart attacks showed that a significant number of them carried a gene for hyperlipidemia (high levels of fat in the blood). This indicated that a single gene could contribute appreciably to the cause of a common, complex disease. More recent studies of tissue cultures derived from affected individuals have shown that there is a gene responsible for lipoprotein receptors on the cell surface, that these receptors are defective in the cells of affected individuals, and that these defects lead directly to increased cholesterol accumulation in the blood, as well as to the clinical manifestation of atherosclerosis, or hardening of the arteries. This demonstrates that a variety of research approaches--in this case, clinical epidemiological studies in human populations and biochemical studies using tissue cultures derived from patients--may be necessary to generate the insights needed to better understand the complex common diseases.

In addition, it has been shown that increased susceptibility to approximately 40 human diseases, including various diseases of the joints, neurological diseases, and cancers, tend to be associated with certain genes that have no currently known intrinsic relationship to these diseases. Other studies have shown some relationship between viral infections and the predisposition toward certain diseases, such as juvenile diabetes. Relationships between genes, viruses, and complex diseases are still poorly understood, but offer intriguing clues for further research.

In an effort to stimulate research in the area of the genetics of common diseases, the NIGMS Human Mutant Cell Repository (a cell bank) has begun, in the past few years, to accumulate cells from carefully selected patients with common diseases, including diabetes and schizophrenia. Currently, the presence or absence of such diseases cannot be demonstrated in tissue cultures. But, it is the hope of the NIGMS that the availability of these cells will ultimately lead to the discovery of abnormalities characteristic of these diseases in tissue culture cells.

Question: To what extent is it possible to screen the population for individuals at high risk of developing these diseases?

Answer: With perhaps a few notable exceptions, this is not now possible. However, it is important to stress that most of these diseases have some tendency to recur in the same family. There are definite genetic components, for example, in heart disease, hypertension and stroke, some forms of mental illness, and cancer. The importance of recognizing these genetic factors stems from the fact that preventive measures (examples are regular health examinations, changes in diet or smoking habits, and exercise) can delay the onset of overt disease or prevent it entirely.

One possibility for population screening in the future may be a search for individuals with some variants of a protein, antitrypsin. The occurrence of these variants is associated with a predisposition to early adulthood emphysema or other pulmonary diseases. Similarly, screening for inherited hyperlipidemias may provide information on a predisposition to heart disease. The importance of such tests would, of course, be in the area of prevention, since individuals at increased risk can try to modify their environments to compensate for inherited conditions.

HUNTINGTON'S DISEASE RESEARCH

Question: Huntington's disease is a hereditary illness that begins in adulthood, usually the mid-thirties or later. By this time, the unsuspecting victim may have already produced offspring, one-half of whom will be afflicted with the disease.

How much money have you spent on Huntington's research over the past five years and what new breakthroughs in the treatment or detection of the disease can you report?

Answer: While the NIGMS does not support a major program of research directly targeted to Huntington's disease, the Institute does play a vital role in facilitating research in this area through its "cell bank." The Human Genetic Mutant Cell Repository, as it is formally known, was established in 1972, and is supported by a contract to store, in the frozen state, cell culture lines derived from patients with a wide variety of human genetic diseases. The function of this cell bank is to provide to investigators well characterized cell lines, free of contamination. The ready availability of these cell cultures facilitates and encourages research that might otherwise not be possible. A subcollection of cell lines in the cell bank is from patients or families with Huntington's disease. This subcollection now contains approximately 150 cell lines and represents an investment of approximately $150,000 over the past few years.

A number of significant studies have been performed using these Huntington's disease cell lines; and, although the basic defect in the disease has thus far proven elusive, some of these studies support the idea that Huntington's disease, like certain other degenerative neurological disorders, may be associated with a defect in the normal repair processes for DNA which has been damaged. Cell lines contained in the National Institute of General Medical Sciences' cell bank are also being used for studies designed to reveal genetic markers that will make it possible to trace the presence of the disease-causing gene before the disease has become manifest.

Question: How is your research on this disease coordinated with that of the Neurology Institute?

Answer: The Huntington's disease subcollection of cells in the NIGMS cell bank has been designed and constructed in collaboration with staff of the National Institute of Neurological and Communicative Disorders and Stroke, the lead Institute for research on Huntington's disease. We expect that consultation and active involvement of that Institute in soliciting or providing additional cell lines to the NIGMS cell bank will continue during the coming year.

CELL RESEARCH

Question: In the December 1980 NIH Research Plan, Fiscal Years 1982-1984, your Institute mentioned a continuing interest in the "exploitation of recent advances in understanding the structure and function of cell membranes." It was also mentioned that due to a number of technical advances in the identification and isolation of membrane components, increased opportunities for progress are now possible.

What progress can you report in this area?

Answer: New knowledge concerning the structure and function of cell membranes is continuing to elucidate both a wide variety of biological functions occurring naturally within the body and the origin of various disorders.

Recent advances in this area include the following:

1. Several important membrane proteins have been isolated and purified. One important example is the "asialylglycoprotein receptor," a membrane protein found on the surface of liver cells, and apparently involved in removing blood proteins which have circulated for a long time and which have lost some of their normally attached sugars. We can now show that these receptors transport the faulty blood proteins into liver cells, where they apparently separate from the spent proteins and then return to the surface membrane of the cell.

2. Another example is the discovery and isolation of a new class of membrane proteins, called the "ribophorins." These proteins are found in the endoplasmic reticulum (a cellular organ) of secretory cells, such as those found in the liver and pancreas; and they have now been discovered to direct the synthesis of certain secretory proteins. Indeed, without the ribophorins, these proteins would clearly not be secreted--an important finding.

3. One membrane protein, known for several years and well studied, is cytochrome p-450. This protein plays a crucial role, among other functions, in drug metabolism within the body. Recently, using recombinant DNA technology, scientists have isolated the structural gene for this protein. The chemical structure of this gene is now being determined, and the information gained will be used to allow a more detailed chemical study of its precise role in the cell membrane.

4. There have also been promising advances in both the development of artificial membranes which mimic living membranes and in understanding the function of the various channels in cell membranes.

   a. It has long been possible to make membrane-like vesicles or films involving two lipid (fatty) layers. Recently, however, researchers have been able to make vesicles which incorporate glycoproteins (proteins containing sugars) into the outer surface only, duplicating the asymmetric structure of naturally occurring membranes, and allowing studies using synthetic membranes under more "life-like" conditions.

   b. It has also become possible to produce vesicles from fragments of normal membranes. These fragments can be selected to contain proteins the functions of which are of particular interest, but which previously could not be studied in a controlled environment. One example involves certain transmembrane channels which allow calcium to pass through under certain conditions. These channels are essential for many normal processes, such as muscle contraction, visual adaptation, and the action of hormones. As a result of the new methodology which has been developed, we have recently learned far more about the physiology and biophysics of how these channels open and close than was previously known.

   c. One type of membrane channel recently investigated by using lipid films has been a fragment (B_{45}) from diphtheria toxin. This channel appears to be of sufficient size to allow the active diphtheria toxin component to enter the cell. Of great interest is the fact that the channelforming fragment seems to require a highly acid environment in order to function.

   d. Another toxin that has recently been shown to form channels in cell membranes is mellitin, the most potent toxin in bee venom. Recent X-ray analysis has shown both how it is possible for this protein to insert itself into a membrane to form a hole in the target cell (thus killing it) and also how it can be stored harmlessly in the venom sac of the bee.

   e. Lastly, over the past few years, the action of cholera toxin has become much better understood. One necessary step for the toxin to become effective is for it to "bind" to a specific type of lipid, known as GM1, in the membrane of target cells. The mechanism by which this attachment occurs has been shown through work supported by NIGMS; and one investigator has recently shown that a toxin from an unrelated organism, *E. coli*, acts in the same way, and causes a mild form of dysentery under certain conditions.

BUDGET

Question: In the present atmosphere of budgetary austerity, what programs have you had to cut back or discontinue because of a lack of funds?

Answer: The NIGMS has proposed a $2.3 million reduction in the budget for its Pharmacological Sciences Program in 1983, as compared to 1982. In addition, the budget includes a reduction of $1.4 million in the Institute's support for research training activities overall, from $46.1 million in 1982 to $44.7 million in 1983. This continues a trend in the reduction of NIGMS support in both these areas since 1981. The President's budget includes a slight increase for the Institute's Physiology and Biomedical Engineering Program (PBME) in 1983, but this is still less than the Institute's budget for this program in 1981 and represents a decision to hold funds for the PBME Program relatively constant.

Question: What impact has this had on your research programs?

Answer: In the face of inflation, budgetary cuts and constant level budgets obviously reduce the ability of the Institute to support the development of new knowledge in given research fields, such as pharmacology. In addition, attempts by the NIGMS to put as much money as possible into areas of great excitement, such as basic genetics research and research in the fields of cellular and molecular biology, have further reduced the availability of funds for research in areas which have proven more stubborn in yielding new scientific information. It is nevertheless recognized that budgetary constraints inevitably require these kinds of trade-offs to be made.

Question: What impact has this had on your training program?

Answer: The number of individuals receiving research training support from the NIGMS has decreased over the past few years from 3,921 in 1981 to 3,471 in 1982, and now to 3,151 in 1983. This has affected all Institute programs, except the Minority Access to Research Careers (MARC) Program, which has continued a moderate level of growth. This will mean a somewhat smaller pool of biomedical researchers about ten years into the future. Nevertheless, a special effort is being made to spend each available dollar wisely, in order to assure that the individuals who do receive support are those with the best potential for having successful careers in biomedical research.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal year 1982 and how much will you spend in 1983?

Answer: In fiscal 1982, we anticipate supporting 20 centers for $11,876,000. The budget for fiscal 1983 proposes funding 19 centers for $10,211,000.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: NIGMS is achieving economies in funding research centers in two ways. First, since 1978, NIGMS has imposed a ceiling on the amount of funds that research center grant applicants may request. This limitation assures that research center grants will not absorb a disproportionate share of the Institute's budget. It also reflects our belief that limiting the number of interrelated research projects in a research center promotes the kind of close collaboration between basic research and clinical research scientists that this type of grant was specifically designed to stimulate.

Second, the fiscal year 1983 budget for research center grants reflects the same percentage cuts for indirect costs as are proposed for regular research grants.

BUDGET

Question: How will the proposed budget affect your program planning for the coming year?

Answer: The key principle governing program planning in the National Institute of General Medical Sciences is a commitment to the support of high quality scientific studies in the most promising areas of basic biomedical research, and this principle will continue to guide the Institute as it sets its program priorities over the coming year. The Institute's long-standing commitments to the investigator-initiated research project grant as a funding mechanism and to multidisciplinary research training will also be reflected in the distribution of Institute funds in fiscal 1983.

Question: Where will you place your priorities?

Answer: Under the proposed budget, NIGMS will continue to emphasize research studies in the fields of genetics and cellular and molecular biology, because these areas have given rise to such exciting discoveries in recent years. So that well-trained, versatile scientists will be available 10 years from now, the Institute also plans to continue to place a high priority on its multidisciplinary research training programs, with primary emphasis on institutional predoctoral fellowship awards.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: While the Institute's relative priorities among its scientific programs remain essentially the same, budgetary constraints together with inflation have resulted in a steady decrease in the number of research project grants that can be funded and the number of trainees who can be supported.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

STATEMENT OF DR. BETTY H. PICKETT, ACTING DIRECTOR

ACCOMPANIED BY:
  DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
  JOEL R. HEDETNIEMI, EXECUTIVE OFFICER
  ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. Our next witness is Dr. Betty Pickett, Acting Director of the National Institute of Child Health and Human Development. Doctor, you are very welcome here. I'd appreciate it if you'd introduce your colleagues and then give us a brief summary of your opening statement. I might remind you your opening statement will be included in the record in its entirety, and if you can summarize it we will have more time for questions and developing cases that we might need to take to the floor.

INTRODUCTION OF ASSOCIATES

Dr. PICKETT. I'd like to introduce on my left Mr. Joel Hedetniemi, Executive Officer of the National Institute of Child Health and Human Development. Directly behind us are Mr. Arthur Fried, Budget Officer of our Institute and Dr. Heinz Berendes, Associate Director of the National Institute of Child Health and Human Development and Director of the Institute's epidemiology and biometry research program. He was formerly Chief of the Contraceptive Evaluation Branch of the NICHD Center for Population Research.

I am very pleased to have the opportunity to represent this excellent Institute at this hearing and will be happy to briefly summarize the opening statement.

The research program of the National Institute of Child Health and Human Development has two major foci: Maternal and child health and population.

The Institute combines studies in basic and clinical biomedical science with a range of related behavioral and social research. Our efforts are aimed at normal human development, from fertilized egg, to infant, to adolescent and adult, and are also aimed at the problems of fertility and infertility, contraception, childbearing, and childrearing.

Much of our research bears on prevention.

For example, one major goal is to reduce infant mortality.

Most of the 45,000 infants who die in the United States each year are born prematurely or are of low birth weight. We place high priority on research directed at preventing prematurity and subsequent infant mortality and morbidity.

We also want to reduce and ultimately prevent birth defects which affect about 150,000 newborns in this country every year. Significant congenital malformations or hereditary disorders are studied from a variety of approaches.

Mental retardation is another major emphasis of this Institute. There are more than 6 million retarded individuals in this country, and 125,000 new cases are added each year.

Many of the Institute's mental retardation studies aim at identifying causes of mental retardation in the hope of ultimately being able to prevent their occurrence.

Advances in fetal and pediatric medicine continue. In our intramural program, scientists have succeeded in developing an animal model for the repair in utero of one severe birth defect, hydrocephalus. Other intramural scientists are among the first to test a new synthetic growth hormone which may soon help thousands of children whose growth is stunted.

In the population sciences, work based on the Nobel Prize winning research of Drs. Guillemin and Schally has led to the development of synthetic copies of a brain hormone that plays a key role in reproduction. Research on these new drugs may ultimately lead to the first safe and successful contraceptive drug for men, and probably as well the first safe once-a-month pill for women.

We continue our efforts to assess the safety and effectiveness of contraceptive methods currently in use and to develop the knowledge base which will yield new safe and effective contraceptives acceptable to a wide range of individuals.

In the behavioral and social science areas, NICHD supports research which includes studies in parent-child relationships; children's language development; intellectual and emotional development, including that of retarded children; children's health behaviors; the impact of changing family size and structure in our society; fertility trends in relation to family planning; and studies of population composition and structure.

To summarize in one sentence, the research we address is related to some of the most significant and costly health problems affecting our society.

Mr. Chairman, the National Institute of Child Health and Human Development requests $233,575,000 for the fiscal year 1983, an increase of $7,266,000 over last year.

I will be glad to answer any questions.

PREPARED STATEMENT

Senator ANDREWS. Thank you, Doctor. I knew we were cutting the budget; I didn't know it was that much. We will insert your prepared statement in the record at this time.

[The statement follows:]

STATEMENT OF DR. BETTY H. PICKETT

The National Institute of Child Health and Human Development supports and conducts research to improve the health and well-being of the developing infant and child and to prevent conditions that have their origins early in life and lead to adult disabilities and early death. Problems associated with reproduction and development such as birth defects, premature birth, and mental retardation, are among the most significant and costly health problems of our society. To prevent or ameliorate these problems, the NICHD supports and conducts a comprehensive research program that combines maternal and child health research with a full range of population studies that focus on the complexities involved in contraception, childbearing and childrearing. The program includes biomedical, behavioral, and social science projects.

Prevention

The events of pregnancy, labor, and birth present the greatest opportunity in medicine for intervention to prevent long-term disability. The management of these events may make the difference between a normal, healthy lifespan and early death or a lifelong disability from cerebral palsy, mental retardation, visual or hearing impairment, or other disorders. Since the NICHD concentrates on reproduction and early development, the Institute is in a prime position to contribute to the prevention of costly health problems.

Birth Defects

Approximately 150,000 infants are born each year in the United States with significant congenital malformations or hereditary disorders. While representing 3 to 5 percent of all births, they account for approximately 20 percent of infant mortality and account for many cases of mental retardation, physical disability, blindness and deafness, and developmental disabilities.

The first cases of successful human fetal surgery reported this year are exciting steps forward in fetal medicine. While the NICHD had no role in these cases involving human patients, NICHD scientists have succeeded in developing a monkey model for the in utero correction of hydrocephalus. In human infants this condition usually results in severe brain damage before birth and subsequent mental retardation. If these surgical techniques and methods of treatment for hydrocephalus in monkeys prove successful in human application by others, a major cause of mental retardation in affected children can be alleviated.

It has long been known that women who are diabetic have an increased risk of bearing children with birth defects. The precise reason for this is not known. The NICHD recently launched a multicenter study to monitor diabetic women before they become pregnant and throughout their pregnancies to determine if careful control of the mother's diabetes during the first three months of pregnancy can reduce the risk of birth defects.

Prematurity

Premature birth is one of the most common causes of neonatal mortality and morbidity. Infants born with low birth weight or after short gestation account for two-thirds of the 45,000 infants who die in the U.S. each year.

Improvements in the treatment of premature infants and other research advances have contributed to a 22 percent decline in infant mortality since 1976, a decline that represents the prevention of some 10,000 infant deaths each year. Yet the very basic question of what triggers the start of labor remains unanswered. If the answer to this question were known, more progress could be made in preventing prematurity.

The NICHD is supporting studies on the biochemical events accompanying the onset of labor. While research has resulted in a promising new drug--ritodrine--for the prevention of premature labor, the search for even more effective drugs is continuing.

One promising line of study investigates the role that infection may play in triggering the onset of premature labor. If infection is found to be a major cause of prematurity, this development could hold great promise for a dramatic reduction in the incidence of prematurity.

Mental Retardation

Mental retardation is one of the most complex and challenging problems related to human development. Often it is the product of multiple, interacting biological, behavioral, and social variables. More than 200 mental retardation syndromes have been identified, and new ones are discovered each year.

Progress is being made against the problem. Mental retardation resulting from one genetically determined defect, phenylketonuria (PKU),has nearly been eradicated with the development of an effective, inexpensive screening test and an effective dietary treatment. Many states now mandate screening for PKU, and admissions of PKU patients to residential institutions for the mentally retarded have been eliminated. An effective screening test for another inborn error of metabolism--hypothyroidism --has been developed and is coming into widespread use. Hypothyroidism, when left untreated, results in severe mental retardation. It now can be diagnosed at birth using the same drop of blood used in PKU screening and treatment is easy and effective. Hypothyroidism is an even more common cause of mental retardation than PKU.

The NICHD research program on Down syndrome, which is the most common and readily identifiable genetic condition associated with mental retardation, is making some inroads into understanding the condition. Institute-supported scientists have succeeded in developing an important research tool--an animal model for Down syndrome. These investigators are selectively breeding mice which produce litters with specific chromosomal abnormalities. Some of the genes known to be located on chromosome 21 in humans have been discovered on mouse chromosome 16. Using this animal model, scientists are able to conduct experiments which would not be feasible using human subjects. The NICHD recently announced the availability of this new animal model to the research community and anticipates an acceleration of research relating to Down syndrome.

Basic Science

Progress in basic science underlies clinical advances in treatment and prevention. For example, until recently study of DNA and recombinant DNA techniques was considered to be in the realm of basic science. But now the first clinical applications of recombinant DNA techniques have begun. Synthetic human growth hormone produced with recombinant DNA techniques is currently undergoing clinical trials. If its safety and efficacy are demonstrated, an unlimited supply of human growth hormone will enable pediatricians to provide better treatment for children with short stature due to growth hormone deficiency. Previously human growth hormone was available only from human pituitaries removed at autopsy, and supply of the hormone was severely limited.

In another approach, important developments are occurring in research with synthetic copies of natural peptide hormones, specifically luteinizing hormone-releasing hormone (LHRH). LHRH is now in transition between basic research and clinical application. A few reports have been received of successful clinical use. For example, the first cure of a rare type of male infertility using LHRH was recently reported, and LHRH has been used on a limited basis to treat certain specific forms of female infertility. NICHD intramural scientists have also used LHRH in the first successful treatment of precocious puberty, a condition in which affected infants and children prematurely begin the process of puberty with the accompanying physical changes.

In a different application, there is evidence that synthetic LHRH has the potential for becoming the first successful contraceptive drug for men and a safe once-a-month birth control pill for women. Very limited clinical trials have started using the drug for these purposes. Early results are promising, but much more testing and development are necessary before LHRH will be available as a contraceptive agent.

Other exciting developments in basic research are being pursued by both Institute grantees and intramural scientists. For example, Institute investigators have discovered the possible mechanism by which the embryo is protected against rejection by the mother's immune system during its first days in the uterus. Transplants of tissue (allografts) from one individual to another unrelated individual are usually rejected, because the recipient's immune system recognizes the transplanted tissue as genetically foreign. For all practical purposes, the embryo is an allograft. Discovery of the proteins which protect against maternal rejection of the embryo may someday contribute to progress in organ transplant surgery, cancer treatment, and in preventing repeated miscarriage in some women.

On another front, an NICHD grantee has recently reported the successful transfer of a "working" gene from an animal of one species (rabbit) to another species (mouse) whose offspring inherited the "working" gene. This research points to the possibility that in the future, genetic disorders caused by absence or malfunction of genes may be corrected through the transfer of healthy genes.

Social and Behavioral Science

The NICHD maintains significant research interest in the behavioral and social aspects of human development as well as the biomedical. Data from NICHD investigations of environmental and nutritional interactions suggest that overall growth and development are affected by variations in social environment and early emotional experience. Infants respond to and interact with their environment at birth, and they are able to learn and communicate long before they can talk. Studies on the development of learning ability make it possible to assess the condition of infants who are born at risk for abnormal development and to evaluate environmental effects on these infants, and to consider the impact of special training programs designed to stimulate their development.

NICHD-supported researchers also study learning disabilities such as dyslexia, an impairment of reading ability. Tests developed with NICHD support are useful not only for diagnosing reading disability but also for prescribing remedial procedures.

The NICHD supports research on adolescent development from various perspectives that include cognitive, emotional, and social development; patterns of interaction with family, peers, and school; and behavioral endocrinology of puberty. This includes research on the social and economic factors associated with adolescent childbearing. There is an association between early childbearing and low birthweight babies and other adverse pregnancy outcomes. Research findings indicate that the risks, especially among the very young, are a mixture of social and biological factors. There is some evidence that high quality prenatal care offsets these risks, but more research on this issue remains to be done.

Important to the research on adolescent childbearing are studies on the factors that lead adolescents into parenthood. Much research needs to be done to understand factors that lead to early sexual activity and the use and non-use of contraceptives.

Future Plans

This brief summary touches on only a few of the many areas of concern to the NICHD. The Institute recently completed an exhaustive evaluation of its plans and programs and from this exercise developed a comprehensive Five Year Plan for the future. One of the features of the Five Year Plan is that it includes an evaluation process to better monitor research progress and to provide a basis for updating goals and research objectives. The plan is in the early stages of implementation.

Budget Request

Mr. Chairman, the National Institute of Child Health and Human Development requests $233,575,000 for fiscal year 1983, an increase of $7,266,000 over last year.

BIOGRAPHICAL SKETCH

Name: Betty Horenstein Pickett, Ph.D.

Date and Place of Birth: February 15, 1926
Providence, Rhode Island

Marital Status: Married to James McPherson Pickett 1952

Education:

1945 - A.B. (Psychology) Magna cum laude, with High Honors in Psychology, Brown University

1947 - Sc.M (Psychology), Brown University

1949 - Ph.D. (Psychology), Brown University (Thesis: Performance of Conditioned Responses as a Function of Strength of Hunger Drive)

Positions Held:

July 1981	Acting Director, National Institute of Child Health and Human Development
July 1979	Deputy Director, National Institute of Child Health and Human Development
January 1979	Deputy Director-Designate, National Institute of Child Health and Human Development
June 1977 - January 1979	Associate Director for Extramural and Collaborative Research Program, National Institute on Aging
March 1977 - June 1977	Associate Director for Extramural and Collaborative Research Program (Designate), National Institute on Aging
July 1975 - March 1977	Acting Director, Division of Extramural Research Program, National Institute of Mental Health
September 1974 - July 1975	Director, Division of Special Mental Health Programs, National Institute of Mental Health
February 1968 - September 1974	Deputy Director, Division of Extramural Research Programs, National Institute of Mental Health
July 1966 - February 1968	Chief, Cognition and Learning Section, Behavioral Sciences Research Branch, Division of Extramural Research Programs, National Institute of Mental Health
August 1963 - July 1966	Executive Secretary, Research Career Program, National Institute of Mental Health
August 1962 - August 1963	Research Consultant to Mental Health Unit, Region #1, Public Health Service, Department of Health, Education, and Welfare
March 1958 - December 1959	Executive Secretary, Behavioral Sciences Study Section, Division of Research Grants, National Institutes of Health
December 1959 - March 1961	Executive Secretary, Experimental Psychology Study Section, Division of Research Grants, National Institutes of Health
March 1961 - March 1962	On leave and resident in Stockholm, Sweden (during husband's year of study at Royal Institute of Technology)

March 1953 - March 1958	Professional Associate, Psychological Sciences, Bio-Sciences Information Exchange, Smithsonian Institution, Washington, D.C.
February 1952 - June 1952	Lecturer in Psychology, University of Connecticut, Department of Psychology
September 1951 - December 1951	Assistant Professor, University of Nebraska, Department of Psychology
September 1949 - June 1951	Assistant Professor, University of Minnesota, Duluth Branch, Department of Psychology

Membership on Task Forces, Committees:

EEO Counselor, NIMH, 1970-1972

Civil Service Commission Board of Examiners, Health Scientist Administrator Panel, 1970-1976; 1981

Special Assistant to the Director, National Institute of Mental Health, for Women's Action Programs June 1971-1972 (Purpose: to establish the NIMH Women's Council)

National Institute of Mental Health Research Task Force, May 1972-November 1974, Co-chairperson Psychology Study Group

Grants Associate Board, Division of Research Grants, National Institutes of Health, 1973-74; 1978-80

Director's Research Advisory Group, National Institute of Mental Health, September 1974-April 1977

Interagency Committee for the Implementation of the Research on Aging Act of 1974, Research and Planning Subcommittee, October 1974-May 1975

Task Force to Study the Research Program of Saint Elizabeths Hospital, July 1975-December 1975 (Task Force Chairperson)

National Institute of Mental Health Outside Work Activities Task Force, March 1976-June 1976 (Task Force Chairperson)

National Institute on Alcohol Abuse and Alcoholism Task Force on Grants and Contracts to National Organizations, June 1976-December 1976

National Institutes of Health Extramural Associates Program, 1978

Chairman, National Institute of Mental Health Search Committee for Chief, Laboratory of Psychology and Psychopathology, 1978

Member, National Institutes of Health, Search Committee for Associate Director for Administration, 1979

Member, National Institutes of Health-Alcohol, Drug Abuse and Mental Health Administration Interagency Committee on Health and Behavior, 1980-

Member, National Cancer Institute Search Committee for Deputy Director, 1980

Member, National Institute of General Medical Sciences Search Committee for Associate Director for Program Activities, 1981

Member, National Institute of Dental Research Search Committee for Director, 1981

Societies:

American Psychological Association
Eastern Psychological Association
Psychonomic Society
Association of Women in Science
American Association for the Advancement of Science

Society for Research in Child Development
Academy of Behavioral Medicine
Sigma Delta Omicron, Graduate Women in Science

Honors:

Phi Beta Kappa, 1945
Sigma XI, 1945
University Fellowship, Brown University, 1947-48
Miss Abbott's Alumni Fellowship, Brown University, 1948-49
A.B., Brown University, Magna Cum Laude, high honors in psychology
DHEW Superior Service Award, 1972
DHEW Distinguished Service Award, 1975
FEW Award for Distinguished Service in Support of Equal Opportunities for Women, 1975
Citation from Graduate School, Brown University, for scientific and professional achievement, 1978
Harold M. Hildreth Award (for distinguished contribution to psychology in the public service, 1979, American Psychological Association)
Elected Fellow, AAAS, 1981
Recipient of SES Bonus Award for Outstanding Performance, 1981

Research Interests:

Experimental Psychology
Research Administration

Publications:

Kimble, G.A. and Horenstein, Betty R. Reminiscence in motor learning as a function of length of interpolated rest. J. Exp. Psychol., 38, 239-244, 1948.

Schlosberg, H., Duncan, M.D., Daitch, Horenstein, Betty R. Mating behavior of two live-bearing fish Xiphophorus hellerii and platypoecilus maculatus. Physiol. Zool. XXII, 148-16, 1949.

Horenstein, Betty R. Performance of conditioned responses as a function of strength of hunger drive. J. Comp. Physiol. Psychol., 44, 210-224, 1951.

Pickett J.M., and Pickett, B.H. Communication of speech sounds by a tactual vocoder. J. Speech & Hear. Res. 6, 207-222, 1963.

BIRTH CONTROL PILL

Senator ANDREWS. Thank you for your statement. I was interested in your talking about the birth control pill. Are you still recommending this morning-after pill as well?

Dr. PICKETT. Are we?

Senator ANDREWS. Or doing work in it?

Dr. PICKETT. No, we are not doing work on the morning-after pill.

Senator ANDREWS. They still have it, don't they? I remember about 7 or 8 years ago——

Dr. BERENDES. Yes.

Senator ANDREWS. I remember when I was on another subcommittee in the House, Dr. Edwards was then head of the Food and Drug Administration, and he told us we couldn't use stilbestrol in feeding cattle. And in my honest life I happen to be a cattle feeder, so that bothered me. I asked him, "Where have you found any stilbestrol traces in the livestock?"

And he said, "Only in the liver, never in the skeletal tissue."

So I said, "I understand 2 weeks after you prohibited the use of stilbestrol in feeding lifestock, you went ahead and OK'd a morning-after birth control pill that contained stilbestrol." He said, "Yes, we did, Mr. Congressman."

I said, "How much of the most grossly contaminated beef liver that you have ever found would a woman have to ingest to equal one of those morning-after birth control pills?"

You know how they line up at the House hearings. They have the people up front, and they have the people with the answers one row behind, and the people with the answers in-depth two rows behind. [Laughter.]

Dr. Edwards turned around to the person behind him and the answer came up, "35, Congressman."

I said, "Do you mean a woman would have to eat 35 pounds of the most grossly contaminated beef liver ever found to equal one of those morning-after pills?"

And then, of course, the message came up from the rear up to Dr. Edwards, and he said, "No, Congressman, 35 tons." [Laughter.]

Then there was another little bit of laughter in the third row and I said, "I've learned a long time ago when there's laughter in the third row there's more of an answer to this question than I have yet."

And, of course, the note came up to Dr. Edwards and he said, "Congressman Andrews, there is; it isn't one pill. It's one pill a day for 5 days."

Then I said, "Well, it's 5 times 35 or 175 tons of the most grossly contaminated beef liver you've ever found to equal one 5-day course of morning-after birth control pill?"

He said, "Yes, Congressman."

And that was the end of our discussion on the morning-after pill and what wonderful things it did, but it stimulated a lot of conversation since.

And I am interested to know we are still using that even though we take a look at it as a carcinogen. And the question, of course, is: At what level does a carcinogen become a carcinogen? And because of the interests of time we are not going to get into that one here, so you are spared that.

Dr. PICKETT. Well, I understand from Dr. Berendes there is no drug licensed for this use at this time.

Senator ANDREWS. There is no drug licensed for that use now?

Dr. PICKETT. Yes.

Senator ANDREWS. So they have gotten away from the approval they gave back then to that particular drug?

Oh, it was never approved, but just under discussion?

Dr. BERENDES. Yes.

Senator ANDREWS. I learn something new every day. I can see the reason why they probably didn't. [Laughter.]

IMPACT OF BUDGET POLICIES

On the budget, the budget proposes to cap indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent, and to maintain training allowances slightly below the fiscal 1982 level.

Dr. Pickett, as I have asked the other Directors, what will these policies do to your research and training efforts, and what will it do to the ability of grant recipients to produce good science and good research?

Dr. PICKETT. Mr. Chairman, my answer is surely consonant with the answers of those who have gone before. These policies will slow our activities. They will certainly make grant recipients more selective as to which research problems they can attack.

But I can say that the 90-percent indirect cost cap in the 1983 budget enables us to make our share of the stabilized grant level. Without the indirect cost cap we would be making 40 fewer research project grants. So it has some utility on our side of the fence. I am sure you will hear different things from those who are the recipients of those grants.

IMPACT OF THE 1982 CONTINUING RESOLUTION

Senator ANDREWS. What has been the impact of the 1982 continuing resolution on your shop, Dr. Pickett?

Dr. PICKETT. Very briefly, we have reduced the number of competing awards by 4 percent, we have reduced the average cost of each competing grant by 4 percent, and we have reduced our noncompeting awards by 2.8 percent—no reduction in numbers but a reduction in dollars.

We have cut our center grants by 6 percent. Other research, which includes that very important research career development program which others have mentioned, is cut by 4 percent. And this reduced support particularly affects the clinical investigator area which is something new we are attempting to develop.

In the training area, institutional allowances have been reduced by 50 percent. The number of trainees has been cut further. And the total dollars have been reduced by nearly 4 percent.

Similar cuts prevail in the research contract area. Our direct operations, intramural and program management activities are cut something between 1 and 2 percent.

PREGNANCY RESEARCH PROGRESS

Senator ANDREWS. Doctor, you mentioned the progress made in treating both the mother and fetus during pregnancy. What specifics can you give us?

Dr. PICKETT. Well, the intramural project, for example, is a rhesus monkey study in which the investigators create a condition like naturally-occurring hydrocephalus—too much buildup of fluid and pressure on the brain, sometimes called water on the brain, and then correct it in utero. They first, of course, carefully locate the position of the fetus in the uterus and then insert a tiny instrument through which a valve can be inserted into the head of the monkey fetus. This valve remains in place throughout pregnancy, and these babies are delivered at term with normal-sized heads.

This is animal work. We are not doing any human work in this area. We understand that investigators in other research centers—not supported by the Institute—have used similar procedures on human fetuses afflicted with hydrocephalus. Other clinicians have done some parallel work in blockages of the urinary system in human male fetuses. One research team has even operated directly on the fetus during pregnancy by opening the uterus, removing the fetus, performing surgery, returning the fetus to the mother's womb, and delivering the baby near term.

So there are some things that we are doing. There are other things that are happening outside of the NICHD, all of which appear to be quite remarkable and very promising for future development.

Senator ANDREWS. Doctor, in this type of research do we have post partum experience as this child developed to, say, 2 years or so, so you can tell what the results of this technique have been?

Dr. PICKETT. The only fetal medicine research in which we might have that experience is in the use of steroids to treat the mother in cases where the fetus has been determined to have immature lungs that would not be able to support the baby after delivery. Treatment of the mother with steroids for some days or hours prior to the actual birth hastens maturation of the lungs and has resulted in babies who are viable.

Studies of those babies within a year after delivery show that they do have healthy lungs. I can't tell you about their subsequent development or child psychology. Those studies have not been made to my knowledge, but it certainly is a field that ought to be pursued.

TEST TUBE FERTILIZATION

Senator ANDREWS. To what extent is your Institute interested in supporting research on human test tube fertilization?

Dr. PICKETT. Our Institute is supporting animal test tube fertilization. We have not been able to support research on human test tube fertilization since 1975 when a policy was established in our department which prohibited that kind of research by us until a report had been made by the President's Ethical Advisory Board. Such a report was made but no official position has been taken by the Department since then.

We did have one application for that kind of research from Dr. Pierre Soupart at Vanderbilt University. No action was taken on that, and Dr. Soupart has since died, and we have had no other proposals.

Senator ANDREWS. Could you provide for the record the text of that Presidential advisory report?

Dr. PICKETT. Yes.

[CLERK'S NOTE.—A copy of the report, "HEW Support of Research Involving Human In Vitro Fertilization and Embryo Transfer," is in the subcommittee file.]

Senator ANDREWS. We have that.

What is your professional analysis of ongoing efforts in this field both in this country and abroad?

Dr. PICKETT. I view these developments with great interest. I recognize the extreme complexity of the procedure and the difficulty with which the positive results we know about have been obtained. We have heard of only one child delivered with a defect, and that was one in Australia, with a cardiac defect which we understand is correctable.

I can't give you a physician's comment on that.

Senator ANDREWS. Let me lead you, then, into a comment that I'd appreciate your making.

Do you feel that this type of research could result in knowledge other than merely supplying the previous childless couple with a child? That is important to them. But could this type of research give us some knowledge that could serve us well in a host of other areas?

Dr. PICKETT. Certainly it would be very helpful to know more about the reproductive process, because infertility is a problem that affects many people and is a tragic problem when it occurs.

We do have an active animal research program in this area, about $3.2 million supporting 42 projects, which is giving us many interesting leads.

However, animal models are just that, and I think I would like my comments to rest at that point.

Senator ANDREWS. Well, the question that I was looking at was the possibility of gaining new knowledge in the development of the cell and the interference with the cell, and that branches off into other things. Could that possibly come from this type of work?

Dr. PICKETT. I'm sure there are many possibilities in this type of work, not only in cellular development but also in the study of the process of implantation by which the fertilized egg attaches itself to the uterus of the mother.

Senator ANDREWS. We can't be off the record but I always like to conduct a hearing to get as good a case as we can when we go on the Senate floor and later on in the conference committee. A lot of people are looking at reductions in the budget and that is necessary. But what we are trying to do here is make as strong a case as we possibly can why the investment in the immediate research we are doing pays off down the line. A lot of people take a look and say, "Oh, this is stuff that isn't that important."

So some of the reasons for the questions are not trying to pry or not to get you to violate your professional ethics. We just want to get on the record as strong a case as we can for the fact that the dollars we are investing in NIH are true investments in the future of mankind, really. I hope you don't think we're going too far afield.

As a matter of fact, we have a report that for every $1 invested in biomedical research, $13 is returned to the economy in terms of longer life and reduced illness.

You've read the articles that go out to the weekly newspapers attacking the funding of the National Science Foundation and some of the "crazy things they do." They have gained the Golden Fleece Award.

What we are trying to do, as I say, is develop a record that the layman can understand as to what we're doing with their tax dollars. And I appreciate the cooperation we've gotten from you and the other witnesses this morning.

SUBMITTED QUESTIONS

Doctor, of course, we have some additional questions that I will give you to be answered for the record. I'd appreciate it if you could provide the answers at the same time that you return the corrected hearing transcript.

It is nice to have you here.

Dr. PICKETT. Thank you.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

NEW BUDGET

Question: The Subcommittee observes that you are due for a $7.2 million increase under the President's fiscal 1983 budget request. How will the increase be distributed?

Answer: The largest portion of the increase, approximately $4.4 million, will cover higher costs of extramural research grants, contracts, and training. The next greatest amount, $2.1 million, provides for increases in Intramural Research, while smaller amounts serve this purpose in Program Management and Direct Operations. By program activity, the respective increases are: Research for Mothers and Children, $805,000; Population, $3,626,000; Intramural Research, $2,130,000; Direct Operations, $638,000; and Program Management, $67,000.

Question: How did you arrive at your priorities?

Answer: We first decided to maintain the basic program objectives and initiatives that have been developed for the NICHD over the past several years, and that no major program components would be terminated in favor of new activities. In this context, then, we allocated the increase primarily to provide for higher costs of non-competing research commitments in the budget mechanisms of research project grants, research centers, other research, contracts, and research training. We also allowed additional funds for mandatory increases in direct operations, program management, and intramural research. With the remaining funds available after all commitments were met, funds were allocated to provide funding for the highest priority competing research project grant and training grant applications, and to provide for needed equipment in the Intramural program.

Question: What is the impact of your plan to fund 107 fewer projects in fiscal 1983? What will be affected?

Answer: The 1983 President's budget provides funding for 252 competing research project grants. This represents approximately 21% of approved applications funded to a 170 priority score. In FY 1982 the NICHD expects to fund 29% of approved applications to 180 priority score; and in FY 1981, 39% were funded to a priority score of 196. The effect of this reduction in the number of competing research project grants will be a lower level of research activity in the maternal and child health areas of high risk pregnancy, clinical nutrition, human learning and behavior, and mental retardation, as well as in population studies in reproductive biology relevant to human fertility and infertility, and the social and behavioral sciences aspects of topics such as childbearing and family structure.

BUDGET

Question: How will the Administration's budget impact upon your Institute in FY 1983?

Answer: The FY 1983 budget of $233,575,000, an increase of $7,266,000, will allow the NICHD to meet its commitments that carry over from FY 1982 and to support selective new and competing continuation projects in both major program areas of the Institute--population sciences and the special health problems of mothers, children, and families.

Question: Will cut-backs take place to the degree that you may have to drop the funding of some programs altogether, or will you trim spending across-the-board?

Answer: Some across-the-board reductions have been made in grants programs, as indirect cost reimbursement on all research project and research center grants has been reduced by 10%, and the average cost of research project grants has been reduced by approximately 4% from original estimates. These measures have been taken to avoid the situation where certain programs would have to be eliminated, and to allow funding of as many new and competing research project grants as possible within the total funds requested.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982 and how much will you spend in fiscal 1983?

Answer: The estimate for NICHD research centers is $24,589,000 in FY 1982 and $26,448,000 in FY 1983.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: Project applications are carefully scrutinized by the investigators before submission to NIH and thoroughly reviewed for scientific merit and administrative conformance by NIH. In this way it will be possible to design a research program to fit within budget limitations.

Research centers have already achieved substantial economies of scale by providing research facilities that can be used by a number of investigators working on different projects and by ensuring collaboration among scientists from a variety of disciplines in seeking solutions to major problems. For these reasons it is clear that research projects conducted in Centers are less expensive and involve the participation of scientists from more disciplines than the equivalent number of projects conducted separately. In addition, the 10% reduction of indirect cost for center grants will result in savings which should not impair essential research and treatment activities.

SELECT PANEL

Question: What recommendations did the Select Panel for the Promotion of Child Health make and what are you doing to implement them?

Answer: The Select Panel made a large number of recommendations in the areas of health protection and promotion, organization and financing of health services, governmental relationships, manpower, and research. The suggestions in the research area included:

1. Calling attention to the importance of research in epidemiology, prevention, social and behavioral aspects of health, health policy, evaluation research, and research on environmental risks to health.

The NICHD supports epidemiological research in maternal and child health as well as in population. The NICHD program is strongly prevention-oriented, with $94,059,000 or 40% of the Institute's budget estimated for prevention in 1983. NICHD support of research in the social and behavioral sciences will be 20% of the Institute's extramural budget in 1983. The NICHD conducts research on the effects of environmental toxins on reproductive health and on genetically-determined susceptibility to environmental toxins. Health policy and evaluation research are outside the scope of the Institute's mission.

2. Calling attention to the need to improve the pool of statistical and survey data on a great variety of maternal and child health issues and to analyze and develop reports from the data already on hand.

Although responsibility for the improvement of statistical data resides with the National Center for Health Statistics and other agencies, the NICHD conducts and supports numerous analyses of existing data on important topics in maternal and child health and population.

3. Recommending that research training opportunities be increased in primary care settings and other settings oriented to health promotion and disease prevention.

The NICHD supports research training in settings oriented to health promotion and disease prevention that deal with such subjects as the causes of mental retardation and the incidence of low birth weight infants.

POPULATION RESEARCH

Question: How much will you spend in FY 1983 in the area of population research?

Answer: The budget activity of "Population," which provides for extramural activities under the various types of research grants, contracts, and training, is estimated at $85,676,000 for FY 1983. The addition of Intramural Research, Program Management, and Direct Operations components of Population research brings the total funding to $101,534,000.

Question: How does it compare with Fiscal 1982? Fiscal 1980?

Answer: The total for Population research will be higher in FY 1983 than in previous years. All population activities of the NICHD are estimated at $96,835,000 for FY 1982, while actual obligations were $86,561,000 in FY 1980.

Question: Is this a funding area of lower priority?

Answer: Definitely not. The population activities received the largest increase in the FY 1983 NICHD budget. Extramural funding -- grants and contracts -- for Population increased by $3,626,000, compared to $805,000 for all other extramural funding. In the important area of research project grants, which accounts for nearly 56% of the total Institute budget, allocations were made toward a goal that the major components of the NICHD--Population and Research for Mothers and Children--will be able to fund equal percentages of approved applications, or, stated another way, that equal priority score paylines will be used, Institute-wide.

NEW CONTRACEPTIVE DRUG

Question: We are aware of your efforts to develop synthetic copies of a brain hormone that could be used as a contraceptive drug for both men and women. Please bring us up to date on this.

Answer: Several clinical trials utilizing these types of drugs have been completed and others are still in progress. Use of these drugs in women volunteers has produced encouraging results for fertility regulation. Additional clinical trials are being initiated in women to focus more narrowly on specific contraceptive approaches. In the human male, the experience has been more limited and the data are less encouraging. However, recognizing the importance of developing a male contraceptive, we are pursuing clinical investigation in male contraception. Additionally, we plan to look in the clinic at another group of related drugs, the so called antagonists, which may offer some additional advantages for fertility regulation. The clinical program is supplemented by ongoing vigorous programs of synthesis and biological testing of additional related compounds.

Question: How far from general public use of this new drug are we?

Answer: The demonstration of high efficacy and safety of these drugs as fertility regulating agents is an expensive and time-consuming process. A minimum of an additional six to eight years is required before these drugs are available to the general public for contraceptive purposes. However, they may be available to the general public sooner for other therapeutic purposes, such as precocious puberty.

DIABETES

Question: We note you are conducting a major study to determine how diabetes causes birth defects. How many people are participating in this study--and when do you expect to have some solid information?

Answer: The NICHD Diabetes In Early Pregnancy project has recruited a total of 372 pre-pregnant diabetic and 480 pre-pregnant control women to date. There have been 123 pregnancies in the diabetic and 175 in the control group. Two factors make it difficult to predict when definitive results will be available: the fertility rates of the study subjects, and the number of pregnancies ending in a fetal loss. Both will have a major impact on the length of time it will take to collect enough information to examine the effects of diabetes on malformations. It is hoped that sufficient data will be available in two to three years.

As this data is being collected, the study is also gathering important information on early fetal loss rates in both the diabetic and normal populations. Preliminary data is already available from the 298 pregnancies thus far. We hope these data will help define the risk of suffering a fetal loss throughout pregnancy.

Question: To what extent is this study being coordinated with the Trans-NIH Diabetes effort?

Answer: This study has been presented to the Trans-NIH Diabetes Coordinating Committee, the Diabetes Mellitus Interagency Coordinating Committee and the National Diabetes Advisory Board. Updated progress reports of this important project are forwarded to those coordinating groups as they become available.

TEST TUBE FERTILIZATION

Question: What is your professional analysis of on-going efforts in the field of test tube fertilization both in this country and abroad?

Answer: Our professional analysis of on-going efforts in the fertilization of human ova _in vitro_ is that the work in this country and abroad is proceeding as well as might be expected given the relative paucity of efforts aimed at maximizing the safety and efficacy of the procedure. Of the more than a dozen births resulting from the procedure, an abnormality has been reported in only one child. And this abnormality, a cardiovascular defect, has been reported to be correctible through surgery. It appears that the most progress in human _in vitro_ fertilization has been made in Australia and England.

TREATMENT IN PREGNANCY

Question: What developmental defects have been successfully treated?

Answer: An exciting advance in the last few years has been the ability to treat developmental defects of the fetus in the uterus. Until recently this treatment has usually involved treating the mother to treat the fetus, but in the last year several teams of investigators have treated the fetus directly for certain developmental problems. One of these problems is urethral stenosis. In this disorder passage of fetal urine from the bladder to the amniotic fluid is blocked. As a result, urine backs up into the kidneys and produces severe, life-threatening damage. This disorder has been corrected in two ways. In most instances a needle has been inserted through the mother's abdomen and uterus into the fetal bladder, with ultrasound guidance. A catheter has then been placed in the bladder through the needle, and left behind to drain urine through the fetus's skin into the amniotic fluid after the needle is withdrawn. In most instances this treatment has been effective in preventing further kidney damage and the infants have survived, but some have died of associated problems. In one case, not yet published, open-uterus surgery was performed to insert the catheter, and the pregnancy continued. The fetus died after birth several weeks later due to other problems, even though the operation was successful. Nonetheless, this landmark operation represents the first true fetal surgery.

A second developmental defect approached surgically in the past year in humans is hydrocephalus. In this disorder too much fluid accumulates within the brain and destroys brain tissue by pressure. Surgeons have treated several fetuses with this disorder by inserting a shunt with a valve through the fetal skull into the fluid-filled cavities of the brain to drain off the fluid and relieve the pressure. They used a needle insertion technique similar to that used for inserting the bladder catheter. The final outcome of these treatments has not yet been published, except to note that the valves worked and stopped the progression of hydrocephalus.

The role of the NICHD in this area of research has been support of some of the basic research in animals to develop the devices and techniques. One of the leading laboratories is that of the Pregnancy Research Branch of the NICHD's intramural program at NIH. Scientists in this laboratory, using a monkey model, have inserted a shunt valve they developed into the brain of monkey fetuses with hydrocephalus. More than 80 percent of the fetuses had a successful outcome, and the monkeys have developed normally after birth without progression of hydrocephalus.

Other developmental problems have also been successfully treated, though in less dramatic fashion. A technique developed and tested by NICHD-supported investigators for prenatal diagnosis and treatment of fetal lung immaturity has helped to reduce the incidence and severity of neonatal respiratory distress syndrome. Two complex genetic metabolic diseases, methylmalonic acidemia and multiple carboxylase deficiency, have been treated successfully in utero by administering large doses of a vitamin to the mother. NICHD-supported investigators are currently assessing a dietary treatment regimen for use in pregnancy to try to prevent the severe developmental problems and mental retardation in infants of mothers with phenylketonuria (PKU). Another NICHD study is focusing on preventing developmental defects in infants of diabetic mothers by rigid control of maternal blood sugar before conception and early in pregnancy. There is also great interest in research reported from the United Kingdom suggesting that neural tube defects (anencephaly and menigomyelocele) can be prevented by giving women folic acid (a vitamin) before conception and during early pregnancy.

Question: How much will you spend on this research in FY 1982--and how much do you plan to spend in the new fiscal year?

Answer: Estimated obligations in FY 1982 are $5,000,000 and in FY 1983, $5,100,000.

SUDDEN INFANT DEATH SYNDROME (SIDS)

Question: To what extent was your Institute involved in the research that led to the discovery of the elevated thyroid hormone in the blood of babies that had died of "crib death"?

Answer: NICHD supports the research that led to the discovery of the elevated thyroid hormone levels (T3) in the blood of babies with "crib death". This work is funded as part of a Major Research Program grant, entitled "Biological and Behavioral Aspects of SIDS," awarded to the University of Maryland.

Question: What is your evaluation of the significance of this finding, and how might it tie in with the future federally-funded research in this area?

Answer: This is an interesting and provocative preliminary finding that has generated a great deal of interest in the biomedical community, since the level of T3 in blood plasma may be an indicator of risk for SIDS. However, these latest findings are still too preliminary to have immediate clinical application. The data obtained must be further evaluated in a scientifically controlled manner to ascertain validity of the data. If evidence from a number of laboratories supports the preliminary results and hypothesis, new SIDS research activities pertaining to metabolic factors associated with SIDS can be anticipated.

Question: What is your planned funding level for SIDS in fiscal 1983 -- and compare it to previous years. Higher? Lower?

Answer: It is estimated that the NICHD will obligate $19,800,000 for SIDS research in FY 1983, higher than any previous year. The estimate for FY 1982 is $19,000,000, and FY 1981 actual obligations were $18,765,900.

CHILD NUTRITION

Question: What is being done to coordinate the Nutrition Research Activities of the NICHD and Baylor University Nutrition Research Center?

Answer: This coordination is achieved through joint activities of the NICHD; the Children's Nutrition Research Center (CNRC) at Baylor University; and the agency that sponsors the CNRC, the Human Nutrition Center of the Science and Education Administration, U.S. Department of Agriculture. Since the initial USDA grant to the CNRC, scientists and administrators of these three organizations have: (1) Signed a memorandum of agreement, July 9, 1979, to participate in joint planning to ensure cohesive and integrated programs of nutrition research. (2) Co-sponsored a symposium entitled " Nutrition of the Child: Maternal Nutritional Status and Fetal Outcome," held October 24-26, 1979, to assess the current state of the art, to analyze data from previous longitudinal studies of maternal nutritional status, and to plan further research in this important area. The proceedings were published as a supplement to the American Journal of Clinical Nutrition, 34, April, 1981. (3) Created a Board of Scientific Counselors which includes representatives from the NICHD, the Children's Nutrition Research Center, and the USDA. This Board has met six times from November, 1978, through December, 1981. At these meetings the staff of the CNRC present their scientific protocols and latest research findings to non-government and NICHD scientists.

The meetings are characterized by discussions and the sharing of scientific plans, protocols, and results. These meetings also contribute to NICHD-USDA cooperation in the area of nutrition research. (4) Undertaken a contract program on studies of human milk, entitled "The Human Milk Bank Research Distribution Center." After this contract was awarded to the Baylor College of Medicine in July, 1978, the principal investigator was subsequently appointed Director of the Children's Nutrition Research Center. To achieve the goals of this contract on human milk banking, scientists from the NICHD and the CNRC have been in frequent contact in person and by telephone for the past four years. The close relationship has been most productive.

Question: To what extent do these overlap or duplicate each other?

Answer: The NICHD-CNRC collaboration has been and continues to be one of cooperation and productivity. The frequent meetings of the Board of Scientific Counselors ensure that the nutrition programs of the two organizations do not overlap or duplicate each other.

ADOLESCENT NUTRITION

Question: To what extent are you funding any research in the area of nutrient requirements for adolescents?

Answer: Adolescence is a time of profound physical transformation. During adolescence, growth rates are attained that are second only to those reached in infancy. The program of adolescent nutrition of the NICHD emphasizes research on: (1) nutrient requirements during the adolescent growth spurt; (2) exercise, lifestyle, and caloric intake as related to the problem of adolescent obesity and to the opposite problem of anorexia nervosa, a disorder involving near cessation of eating; (3) the special needs of the pregnant adolescent; and (4) dietary habits of adolescents. Currently, the NICHD supports thirteen research projects in the area of adolescent nutrition for a total of $1,134,316 (FY 1981).

Question: To what extent are you funding any research on the special nutritional requirements of pregnant adolescents? What does this research show?

Answer: The NICHD has had a longstanding research interest in the area of the special nutritional requirements of pregnancy, especially in the very young mother. In FY 1981, one project received funding of $29,160 in this area of research. However, within the recent past, the NICHD has funded several large longitudinal studies of nutrient intake and pregnancy outcome. These studies show that a pregnant woman requires at least 70,000 calories above her normal caloric intake during her pregnancy. This has been found to be true in adolescents as well as in more mature pregnant women. This finding means that a pregnant adolescent requires about 300 extra calories per day above her prepregnancy intake.

In the United States during 1979, the latest year for which data are available, 39,000 babies were born to adolescent mothers 15 years old or younger. In this age group the rate of premature births is more than twice that experienced by mothers who are 20-24 years old. [Adolescents older than 15 years who receive adequate prenatal care can expect to have no greater a rate of obstetrical problems than adult women.] Research has recently shown that rates of premature deliveries among pregnant adolescents who are 14 and 15 years old can be greatly reduced by improved nutritional and medical care during their pregnancies.

Research funded by the NICHD from FY 1978 - FY 1980 on diet, life style, weight gain, and gain in lean body mass during pregnancy has disclosed that pregnant teenagers often have unhealthy lifestyles characterized by smoking (among 75% of those in the study), alcohol consumption (33%), and poor diets (30%). Dietary abnormalities include low intakes of folate, vitamin C, and protein as well as excessively high intakes of calories.

The results of this research indicate that the pregnant adolescent has the same nutritional requirements as older pregnant women. However, it seems clear that the pregnant adolescent who is 15 years old or younger has more difficulty in meeting these requirements, particularly in regard to vitamin intake. This difficulty is often attributable to naivete and appears to be remediable, in large measure by improved prenatal nutritional counseling and care.

Question: How many research grant applications are you funding with regard to adolescent nutrition as it relates to eating habits?

Answer: Six research grants that address this topic are currently funded ($385,084, FY 1981). All are concerned with some aspect of adolescent eating habits: (1) Diet and Age at Menarche. This longitudinal study of over 1000 girls examines the influence of strict vegetarianism during childhood and adolescence on the onset of menarche. (2) Developmental and Societal Issues in Anorexia Nervosa. This project addresses the factors that are associated with the eating disorder known as anorexia nervosa, almost total aversion to food and a near cessation of food intake which affects as many as six of every hundred adolescents. Girls are affected nineteen times as often as boys. (3) Childhood Obesity and Past Environmental Factors. This is a study of obesity in young adolescents. An analysis is being made of their lifestyles and eating habits to learn more about specific dietary and other behavioral factors that lead to adolescent obesity. (4) Childhood Obesity: Long-term Behavioral Change. This project addresses the problem of modifying deleterious eating behavior in obese preadolescents and adolescents. (5) Home Based Behavioral Program for Obese Children. This project aims to improve the eating habits of obese young adolescents by the use of a "traffic-light diet," a system of color-coding of foods according to caloric density, green being least dense, red most dense, and yellow in-between. (6) Nutrition Education Research. This part of a large center grant is devoted to research on developing effective programmed nutrition education packages for use by high school students. These teaching materials are intended to instruct adolescents in the basic facts of nutrition.

PUBLIC INFORMATION

Question: Institute information programs include a wide variety of methods that have been used to inform pregnant women about nutrition, smoking, alcohol consumption, etc. To what extent will your public information programs or campaigns be curtailed in the coming fiscal year because of budgetary considerations?

Answer: Budgetary considerations will have no significant impact on NICHD information programs. There will be some reduction of activity due to new Administration guidelines on publications and printing of public information materials.

BUDGET

Question: How will the proposed budget affect your program planning for the coming year?

Answer: The proposed budget will not affect our basic program planning for the coming year. We will be able to maintain all of our ongoing programs and to pursue limited new initiatives in both the population sciences and studies of the special health problems of mothers, children, and families.

Question: Where will you place your priorities?

Answer: Considering broad budget activities, our first priority is on extramural investigator initiated research--supporting the greatest number possible, within the budget, of the so-called research project grants. Here, we will meet our continuing commitments from the previous year, and then make awards for projects that have been rated nearest the top in our highly competitive grant review process. Closely coordinated with this activity is the support for a critical mass of research centers, with their emphasis on economies of scale in the conduct of research, clinical investigations, and translation of new knowledge to medical practice. High priority program topics include high risk pregnancy and infancy, mental retardation, problems in child development, fertility and infertility, and behavioral aspects of childbearing.

Research and development contract activities have been identified for emphasis, in support of developing new and improved methods of contraception and studying the safety of methods already in use. Also, we have allocated resources to sustain the productivity of our important program of intramural research.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: Budgetary restrictions and inflation have not changed our research and educational priorities. Rather, the level of effort--the amount of research or education that can be accomplished--will have to be adjusted to the budget, with every opportunity taken to make the most efficient use of the resources that are available.

NATIONAL EYE INSTITUTE

STATEMENT OF DR. CARL KUPFER, DIRECTOR

ACCOMPANIED BY:

DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
EDWARD McMANUS, DEPUTY DIRECTOR
ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. Our next witness is another scientist well-known to this committee, Dr. Carl Kupfer, Director of the National Eye Institute. Dr. Kupfer, you are very welcome here. I'd appreciate it if you'd introduce your colleagues and proceed with a brief summary of your opening statement which, as you know, will be included in full in the record.

INTRODUCTION OF ASSOCIATES

Dr. KUPFER. Thank you, Senator.

To my left is Mr. Edward McManus, who is the Deputy Director of the National Eye Institute; and directly behind me is Dr. Ronald Geller, the Associate Director. To his left is Mr. Kenneth Cooke, the Executive Officer; and to his left is Ms. Carmen Richardson, Budget Officer.

PROGRAM PLANNING

Perhaps it would be appropriate to mention first the backdrop against which the National Eye Institute fosters research aimed at improving the prevention and treatment of blinding eye disorders. There are approximately 11.5 million Americans who suffer visual impairment at a cost to our Nation of approximately $10 billion a year. To insure that the resources we receive from Congress are used as effectively and economically as possible, the National Eye Institute has made research planning the strong foundation upon which our research program is built.

I think it is particularly appropriate to talk about planning at this time because the National Eye Institute has just completed its third planning cycle. We are concerned with identification of the most important scientific needs in our research programs and, perhaps even more important, the opportunities that are presented to address these needs.

We certainly are concerned that the needs that have been identified relate to the major public health problems that confront us with blinding and disabling eye diseases, from retinal disease, glaucoma, cataract, corneal eye disease, strabismus, and amblyopia. But at the same time we must determine where the opportunities to solve these problems lie.

The basis of our program planning process is to try to determine which areas of research have the highest probability and the greatest potential for solving these problems, and then to determine which of these opportunities should be given priority for funding.

Our program planning activity then allows us to see which research areas need additional resources, which research areas are adequately funded, and which research areas have reached the point where support can be decreased over a period of time.

In addition, I think the documents that result from the program planning process provide an important element for our National Advisory Eye Council in determining the program relevancy of the research grants they review.

From a research point of view, one often is asked what is the role of program planning. We believe that it does speed up the research process. What was going to happen in time will probably happen much more rapidly as a result.

UVEITIS

A good example of this is recent research on uveitis. This is a disease which involves about 10 percent of all visually impaired people in the United States, and it was identified as a research priority in our previous program plans. It was determined that emphasis on immunological research was necessary. This came about, and within the last 3 years not only has a better understanding of this disease been gained but, even more impressively, a promising new therapy has been developed.

If I may just digress for a moment, perhaps you would find it interesting to review some of the aspects of this particular problem.

This [indicating] is a cross section of an eye, similar in appearance to slicing an orange in half, and as you can see, this [indicating] is the front of the eye, the clear cornea. Light passes through the cornea and the lens, which focuses the beam of light on the seeing part of the eye, the retina.

In uveitis, inflammation occurs not only in the retina, but also in the front of the eye.

And this [indicating] is a photograph of a patient who has such an inflammation in the eye which is so severe that it has caused pus to collect at the bottom of the eye. And you can see this white material [indicating], the pus that is trapped due to the severe inflammation in the eye.

The development of uveitis can now be simulated very well in animals and, as a result of animal studies, a new therapy has been developed using a drug, cyclosporin A.

This photograph shows an eye [indicating] that has retinal inflammation. These white spots represent the areas of inflammation. Following treatment with cyclosporin A there is marked improvement in the appearance of the retina as well as improvement in vision.

In addition to finding ways to treat eye disease, we are particularly interested in its prevention. This has been our highest research priority. Recent advances in the prevention area are detailed in my opening statement.

It is easy to see how clinical studies can lead to improved means of prevention. But I'd like to give you an example of how even the most basic research may eventually yield clinical dividends.

NOBEL PRIZE WINNERS SUPPORTED BY NEI

As an example, I would like to cite the work of two long-time National Eye Institute grantees who shared the 1981 Nobel Prize in medicine, Dr. Torsten Wiesel and Dr. David Hubel. Over the past dozen or so years, these neurobiologists have explored the manner by which light falling on the retina in the eye is translated into active seeing by the brain.

Not only have they done this in terms of elucidating the basic mechanisms but, even more importantly from a clinical point of view, they have explored the way the two eyes interact in forming a single image in the brain. As a result, their basic research has had impact on the field of amblyopia, popularly called lazy eye in which there is a decrease of vision; on strabismus, where the eye turns in or turns out; and on the restoration of vision in young infants who are born with a cataract which prevents light from reaching the retina.

So again we see that the most basic kind of research can lead to important new clinical applications.

In summary, the National Eye Institute is requesting $131,550,000 in fiscal 1983.

I'd be happy to answer questions.

PREPARED STATEMENT

Senator Andrews. Your prepared statement will be entered in the record at this point.

[The statement follows:]

Statement of Dr. Carl Kupfer

More than 11 million Americans are visually impaired, and half a million are legally blind. Each year, visual disorders cost our Nation at least $10 billion. To reduce this heavy toll, the National Eye Institute (NEI) fosters research to improve the prevention and treatment of blinding eye diseases and other disorders affecting the visual system. And, to ensure that the resources placed under its stewardship by Congress are used as effectively and economically as possible, the NEI has made research planning the strong foundation upon which our program is built.

Planning for Vision Research

Now is a particularly appropriate time to discuss the NEI's program planning efforts because we are about to complete a document that will serve as a guide for the development of our program through 1987. This new national vision research plan, to be published this spring, will be the result of more than 2 years of effort by the National Advisory Eye Council, the NEI staff, and six panels of distinguished scientists representing all the major fields of vision research and drawn from every region of the country. The new plan defines each major area of research and summarizes advances of the past few years. It spells out program goals and objectives, identifying areas where research is needed most and where the opportunity for sight-saving discoveries is greatest. It recommends priorities for both ongoing research and future program development, assesses the resources needed to carry out these recommendations, and advises the NEI on the best allocation of these resources.

Like the earlier vision research plans published in 1975 and 1978, the new plan will serve as a basis for decision-making by the Council and the executive staff of the NEI. The Council will use the plan during the final stage of the grant application review process to make sure that choices between closely competing grant proposals are made in a most rational manner. Also, the NEI staff will be using the plan as a guide in making decisions on such matters as special projects to be undertaken, allocation of staff time, and use of intramural scientific resources. Finally, because the plan summarizes the thinking of the leaders of the vision research community, we expect that it will be used by scientists in laboratories and clinics across the country. Thus the priorities identified in this plan will influence the course of vision research for the next 5 years, and perhaps even beyond.

Impact of Planning: Uveitis Research as an Example

The manner in which research planning can help hasten scientific advances in a particular field is well illustrated by recent progress in our understanding and treatment of uveitis. This inflammatory disease of the inner eye is responsible for about 10 percent of all visual impairment in the United States. Uveitis was identified as a research priority in the first vision research planning report of 1975 and given even greater emphasis in the 1978 plan. These plans suggested that concepts and techniques from the rapidly developing field of immunology should be more extensively applied to clinical problems involving the eye and cited uveitis as a disease whose treatment might be improved through advances in immunology.

To further stimulate research on uveitis and other eye disorders that might involve the immune system, the NEI also sponsored a series of three workshops on ocular immunology. As a result, proposals for studies of the natural history and possible immunological causes of the disease were submitted by several investigators, and many of these studies have now been funded by the NEI. Scientists in the NEI's intramural program developed an animal model for one type of uveitis, to clarify its mechanisms and to lay the groundwork for laboratory tests of new treatments.

Now we are beginning to realize clinical dividends in this research area. Our intramural scientists have identified and are currently testing a drug that offers hope of controlling uveitis with fewer harmful side effects than conventional medications. The results obtained with the first few patients appear quite promising. Thus it is clear that the planners were correct 7 years ago when they forecast that an immunological approach to the study of uveitis would be particularly rewarding; and their recommendations have undoubtedly stimulated the pace of progress in this area, to the great benefit of uveitis patients.

Prevention of Eye Disease

The ultimate goal of all vision research supported by the NEI, and the highest priority identified in every planning report thus far, is prevention of serious eye disease. Success in prevention could not only save people from visual loss but also from the fear, discomfort, and expense so often associated with sight-threatening disorders.

Research conducted during the past year has raised our hope that measures may be devised to prevent two eye diseases which are of enormous public health significance. These are: diabetic retinopathy, the leading cause of new cases of blindness among middle-aged Americans, and aging-associated (senile) cataract, which causes more cases of visual impairment and is responsible for more eye operations than any other disorder.

Hope for the prevention of diabetic retinopathy comes from research on aldose reductase, an enzyme that normally is present in many of the body's tissues and is believed to be responsible for much of the tissue damage that occurs in people with diabetes. In my testimony of previous years, I explained how the harmful role of aldose reductase was first discovered by NEI scientists studying a particular type of cataract that develops in diabetic laboratory animals. I told you how these scientists developed the first aldose reductase inhibitors--drugs which block the action of the enzyme. The scientists then proved that the most powerful of these drugs could completely prevent the development of these so-called sugar cataracts, even in the presence of uncontrolled diabetes. More recently, the same investigators have conducted studies which suggest that the drugs may improve the rate of corneal healing in diabetics recovering from a sight-restoring operation called vitrectomy. Also, scientists from outside the field of vision research have shown that aldose reductase inhibitors can restore normal function to nerves damaged by diabetes. All of these findings suggest that the inhibitors may be able to prevent diabetes-associated problems in any tissue where aldose reductase is active.

Recently, NEI-supported studies have confirmed that aldose reductase is active in the retina. This finding has given us reason to believe that the enzyme may play a role in diabetic retinopathy, as well as in the other complications of diabetes mentioned above, and that treatment with aldose reductase inhibitors might prevent the retinal disease. The NEI is now making plans for a clinical trial to test the effectiveness of aldose reductase inhibitors as preventives of diabetic retinopathy. The subjects of the study would be juvenile diabetics, who now stand a 50 percent chance of developing the retinal disorder within 7 years after the time that diabetes is diagnosed. Prevention of diabetic retinopathy in this highly susceptible population of diabetics might point the way to a dramatic reduction in the incidence of this eye disorder and blindness caused by it.

In the case of senile cataract, recent studies have shown that the disorder may result from long-term oxidative damage to the lens, possibly arising from lifelong exposure to oxidative agents in the environment. Further studies of the effects of these agents on lens proteins, and of the normal antioxidant defenses of the lens, may lead to ways of preventing senile cataract. Development of even partially effective preventive measures would be of great significance, both in human terms and economically. A treatment which would delay the development of senile cataract by 10 years on the average would reduce by an estimated 45 percent the number of cataract operations performed each year, for a saving of about $530 million annually.

Progress in Other Areas of Clinical Research

In addition to these efforts to prevent serious eye disease, the NEI supports other research aimed at improving the treatment and diagnosis of a wide range of visual conditions. For example, NEI grantees are seeking better ways to substitute for the eye's natural lens, which is removed when a person undergoes cataract surgery. For decades, various types of glass and plastic lenses have been used to help these patients see after the operation. Unfortunately, none of these man-made lenses is entirely satisfactory. Many elderly people have difficulty adjusting to cataract eyeglasses; they may also have problems handling or wearing contact lenses; and they may be reluctant to accept the somewhat increased risk of post-surgical complications that accompanies implantation of an artificial lens within the eye. For these people, research has now yielded a promising new surgical method of correction that does not involve use of any kind of artificial lens. The method, which is still under investigation, is called epikeratophakia. In this procedure, a small piece of corneal tissue from an eye donated to an eye bank is frozen and shaped on a lathe to make a "living contact lens." The piece of tissue is then fitted onto the front of the patient's cornea, permanently changing its shape and helping it to focus rays of light onto the retina. Thus, the sharpness of the patient's vision is improved, but with a piece of natural tissue rather than a glass or plastic lens.

Progress has also been made in developing drugs to protect the eye from damage by the herpes simplex virus, the most widespread infectious agent in the United States. Each year, about half a million people experience painful ocular symptoms caused by herpetic infection of the cornea, the clear tissue at the front of the eye. Severe or repeated infections can cause corneal scarring and blindness. Drugs developed with NEI support have been found effective against herpes, and one of these compounds--vidarabine--has become the drug of choice in treating herpes encephalitis as well. Taking this research one step further, other antiviral agents, including interferon, are now being developed and tested against ocular herpes infections. A major goal is to eradicate latent virus, thereby preventing recurrences of the active disease.

Basic Research in Neurobiology

Most of the examples of progress in vision research which I have cited have been clinical advances. But underlying this clinical progress, and essential to its continuation in future decades, is another activity of vital interest to the NEI--and that is basic research. Since its establishment, the NEI has supported research on the basic processes underlying normal and abnormal vision; these include the manner in which the retina and the brain process visual information and the mechanisms which enable the two eyes to work in coordination with each other. Such studies may take years to pay off in clinical advances, but the potential dividends are enormous.

As an example, I would like to cite the work of two long-time NEI grantees who shared in the 1981 Nobel Prize for Physiology or Medicine. The two, Drs. David Hubel and Torsten Wiesel of Harvard University, spent many years studying the organization and function of that part of the brain responsible for fitting together incoming visual signals to form a visual image of what is seen in the outside world. Among the discoveries arising from this work was that in early life the brain must have clear, compatible images from each eye if it is to develop the ability to fuse the input from both into a single image. Translated into clinical situations, the results of their basic research suggested that an eye which is clouded from birth by a cataract or turned inward or outward because of a muscle imbalance (strabismus) should be treated while the child is still quite young if normal vision is ever to be achieved. Delay of treatment can result in permanent amblyopia, a condition in which the brain ignores the image from one eye and relies exclusively on the other eye as a source of information. Many children have been saved from lifelong blindness in one eye because these basic studies of the visual system revealed the need for early treatment of congenital cataract and strabismus.

Given this strong commitment to basic research, a vigorous program of clinical research, and a well developed planning process to ensure that both are directed toward areas of particular need and opportunity, I am confident that the NEI will be able to continue reporting progress in the fight against eye disease and blindness for many years to come.

In conclusion, Mr. Chairman, to support a continuation of these and other vision research activities in the coming year, the NEI's budget request for FY 1983 is $131,550,000.

BIOGRAPHICAL SKETCH

Name: Carl Kupfer, M.D.

Date & Place of Birth: February 9, 1928 - New York, New York

Citizenship: United States

Marital Status: Married

Education:

June 1945 - Graduated from High School
June 1948 - A.B., Yale University
June 1952 - M.D., The Johns Hopkins Medical School

Board Certification: American Board of Ophthalmology, 1958

Brief Chronology of Employment:

1952 - 1954	Internship and Assistant Residency, Wilmer Eye Institute The Johns Hopkins Hospital
1953 - 1954	Laboratory Assistant, Biostatistics, The Johns Hopkins School of Medicine
1957 - 1958	Research Fellow in Ophthalmology, Wilmer Eye Institute The Johns Hopkins Medical School Laboratory Assistant, Biostatistics, The Johns Hopkins Medical School
1958 - 1960	Research Fellow in Ophthalmology, Harvard Medical School
1960 - 1962	Instructor in Ophthalmology, Harvard Medical School
1962 - 1966	Assistant Professor of Ophthalmology Harvard Medical School
1966 - 1970	Professor and Chairman in Ophthalmology, University of Washington School of Medicine; Research Affiliate, University of Washington Primate Center
1970 -	Director, National Eye Institute National Institutes of Health

Military Service:

United States Air Force, November 27, 1954 - November 26, 1956

Societies:

American Physiological Society
Association for Research in Vision and Ophthalmology
American Academy of Ophthalmology
American Ophthalmological Society
Pan American Ophthalmological Society

Honors and Other Special Scientific Recognition:

Henry Strong Denison Scholarship 1949-1950
Consultant to Blind Babies Home, Boston, Massachusetts, 1962-1966
Program Director, Ophthalmology Training Grant, Massachusetts Eye and Ear Infirmary, 1962-1966
Member, Vision Research Training Committee, National Institutes of Health, 1963-1964
Member, Neurology Program - Project B, National Institutes of Health, 1967-1969
Member, Advisory Committee of Basic and Clinical Research, National

Society for the Prevention of Blindness, Inc., 1968-
Editorial Board, Investigative Ophthalmology, 1969-1977
Clinical Associate Professor, Howard University, Division of Ophthalmology, 1970-
Editorial Board, American Journal of Ophthalmology, 1971-
Member, Scientific Advisory Committee, Fight for Sight, 1971-
Member, Scientific Advisory Panel of Research to Prevent Blindness, 1971-1974
The Secretary's Special Citation, Department of Health, Education, and Welfare, April 1972
Sanford R. Gifford Memorial Lecture, May 1972
The Superior Service Award, Department of Health, Education, and Welfare, May 1974
Ticho Memorial Lecture, September 1974
Member, National Diabetes Advisory Board, 1976-
Migel Medal, American Foundation for the Blind, October 28, 1976
Edwin B. Dunphy Lecture, June 1977
Public Service Award in Ophthalmology, American Academy of Ophthalmology and Otolaryngology, October 1977
Speaker, Academy of Medicine of Washington, D.C., Winter Meeting 1980
Sixth Lorand V. Johnson Lecture, April 1980
Principal Speaker for Friends of Eye Research, Rehabilitation and Treatment at the Helen Keller Centennial Congress, June 25, 1980
C. Dwight Townes Memorial Lecture, March 1981
Speaker, Medical College of Wisconsin Eye Institute Resident Alumni Meeting, June 1981
Speaker, Symposium on Basic Aspects of Glaucoma Research, Anatomic-Institut, University of Erlangen-Nurnberg, Germany, September 1981
Speaker, 35th Annual Congress of Japanese Clinical Ophthalmology, Juntendo University School of Medicine, Tokyo, Japan, November 1981
Speaker, Glenn A. Fry Award Lecture, American Academy of Optometry, December 1981

International Appointments:

Member, Board of Trustees, Helen Keller International Incorporated, 1975-
Chairman, Projects and Priorities Committee, International Agency for the Prevention of Blindness (IAPB), 1975-
Coordinator for USA, US-Japan Collaborative Agreement in Vision Research, 1976-1982
Organizer, Oxford Assembly, IAPB, 1978
Member, International Vitamin A Consultative Group (IVACG), WHO, 1973-
Visiting Professor, Pan American Ophthalmological Association, October 1975
Member of US Delegation to World Health Assembly, May 1978
Member, Advisory Group for Prevention of Blindness Programme, WHO, 1978-
Consultant, Pan American Health Organization (PAHO), 1978-
Temporary Adviser, WHO Task Force on Data on Blindness Meeting, Geneva, November 1978
Participant, Meeting on the Role and Functions of the National Institutes of Ophthalmology, Brussels, December 1978
Coordinator for USA, Priority Area "Eye Diseases," US-USSR Program for Health Cooperation, 1978-1981
Member, WHO Expert Advisory Panel on Trachoma and Prevention of Blindness, 1979-1984
Short-Term Consultant to Regional Office for South East Asia, WHO, New Delhi, India, December 1979-January 1980. Assignment to evaluate the Indian Plan for the prevention and control of blindness and to advise on training and research activities.
Consultant to WHO for Defining Guidelines for Blindness Prevention Programs in Africa, Bamako, February 24-27, 1980
Speaker, General Assembly of the World Council for the Welfare of the Blind, Antwerp, August 1979
Director, WHO Collaborating Center for the Prevention of Blindness, National Eye Institute, Bethesda, MD, 1979-

RESEARCH AND TRAINING EFFORTS

Senator ANDREWS. Doctor, as I have asked the other Directors, the budget proposes to cap indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent. What will these policies do to your research and training efforts, and what will it do to the ability of grant recipients to produce good science and good research?

Dr. KUPFER. We have used the information generated by our program planning to determine those areas where the level of funding can remain constant as well as those areas where there may be some decrease in funding without substantially impeding research progress. Accordingly, we have reduced the cost of our research grants an average of 4 percent, taking into account the priorities identified by our program planning process.

So I think for this one year, fiscal year 1982, we will be able to maintain the momentum of the most important programs.

I think this is also true of research training, but I stress that this is a 1-year, short-term solution.

PRIORITIES OUTLINED IN 1983-87 PROGRAM PLAN

Senator ANDREWS. I was asking about 1983, Doctor. But along the line of program planning, how do your research priorities for the next 5 years differ from those outlined in the 1977 to 1982 planning?

Dr. KUPFER. There is, in some instances, a continued emphasis on what has been identified in the 1977 plan. For example, the areas of immunology and genetics are still stressed.

However, new areas are emphasized that reflect current perceptions of the most urgent needs in vision research. Just to give one example, the area of molecular biology for the first time is being very strongly stressed, in the hope of stimulating the application of this exciting new area of science to the solution of problems important to vision research.

Our concern with the epidemiology of eye diseases has increased so that more stress is being placed on epidemiology. We are very much concerned, for instance, in determining the risk factors that lead to the development of cataract, one of the major causes of blindness in the United States.

Senator ANDREWS. Well, Doctor, in your last 5-year plan, it notes here, your research priorities were retinal diseases, corneal diseases, cataract, glaucoma, and sensory and motor disorders of vision.

Dr. KUPFER. Yes, sir.

Senator ANDREWS. Are you retaining those same research aims? So far you haven't mentioned any one of them.

Dr. KUPFER. Yes, sir; well, perhaps I should explain that those disorders are the five main causes of blinding and disabling eye disease—retinal disease, cataract, glaucoma, corneal disease, and sensory motor disease. They also are the names of our five major research programs, and their ultimate conquest is our long-range goal.

Within each of these categories we have identified specific needs and opportunities for research that we believe will lead to the development of new approaches to conquering these five causes of blindness.

For instance, let me take the example of cataract. This is a main cause of blinding eye disease, and although we have successful operations to treat cataract, I think most people would rather not undergo surgery. We know if we could slow down the course of cataract development by 10 years, we would reduce by about 45 percent the number of people requiring surgery. So our emphasis in the cataract program is to develop ways of prevention, slowing down the development of cataract.

Now, 5 years ago in our second program plan, we were not as aware as we are today of some of the possible risk factors that might lead to the acceleration of cataract development. So in our third program plan we have identified new opportunities for research on such risk factors for cataract that should be pursued very aggressively. These include the effect of ultraviolet light, the effect of ionizing radiation, and perhaps even the effect of certain nutrients in our diet.

SENSORY AND MOTOR DISORDERS OF VISION

Senator ANDREWS. What results are you getting in your motor disorders of vision? You mentioned that as one of your priority items. What have you been able to develop in that line?

Dr. KUPFER. I think there's been a marked change in the approach of the ophthalmologist to the treatment of both amblyopia, which is the decrease in vision in an eye that appears to be perfectly normal in all respects, and in strabismus, in which the eye turns in or out, as well as of cataracts in infants. Many of the changes in the approach of the clinician have resulted from basic research. We now know if we are to treat these conditions effectively it must be done as early as possible, perhaps as early as the first 2 or 3 months of life.

In addition, once the child's vision is corrected surgically, there must be very intensive followup. For instance, fitting contact lenses to infants 2 to 3 months of age following cataract surgery appears to be very important if vision is to develop normally. A scant 5 years ago this was not as well appreciated. And, in fact, the technology to fit these contact lenses was not as well advanced.

NEI CONSTRUCTION

Senator ANDREWS. Doctor, you mentioned a moment ago the construction money. You received $3 million in construction money in fiscal 1980. Yet, we understand you are only now preparing to award the money.

Dr. KUPFER. Yes, sir.

Senator ANDREWS. Why has it taken so long to make this money available?

Dr. KUPFER. Well, first of all, it was necessary to develop guidelines. This was the first time that funds were made available to National Eye Institute grantees for construction and guidelines had to be developed. This was a major undertaking. Fortunately, we had the help of the National Cancer Institute in developing these guidelines. The NCI had had quite a bit of experience in this area.

Second, it was necessary to announce the availability of these funds and to solicit proposals. And we must give the potential grantee institutions a fair amount of time to prepare these very complicated documents to justify why they should be given construction funds.

The announcement, itself was somewhat delayed because of a number of administrative problems, so that perhaps it didn't go out as rapidly as possible.

Senator ANDREWS. Well, when are they going to be finally awarded?

Dr. KUPFER. They have been awarded, sir, at the last National Advisory Eye Council meeting about 3 or 4 weeks ago. All funds have now been committed.

[CLERK'S NOTE.—The Department of Health and Human Services has requested insertion of the following statement in the record: Dr. Kupfer's statement that the grants have been awarded is not the exact technical terminology that should have been used. Dr. Kupfer should have stated that all of the funds have been committed to individual grantees.]

Senator ANDREWS. That is the first we've heard of it.

If you withheld expenditure of this money for so long, did you defer it under the terms of the budget?

Dr. KUPFER. As I understand it, this money was no-year money and, therefore, could be carried from year to year until we were able to obligate it. It was recognized by the Congress that it would take time to make this money available to the community.

Senator ANDREWS. I am told that it wasn't recognized by the subcommittee that it would take 3 years to make it available. The subcommittee felt that when the request was made, there'd been a good deal of thought given to the procedure under which the money would be put out, and that it would be put to contract in a relatively shorter length of time. Now, of course, you are going to end up with about half the building that the committee anticipated getting when it advanced those funds.

And the committee is somewhat concerned over what your plans are for the $3 million you have earmarked for eye money in the current fiscal year. Does this look for another 3- or 4-year dragout?

Dr. KUPFER. Perhaps the representative of HHS would like to speak.

Senator ANDREWS. Sure.

Mr. ITTEILAG. Mr. Andrews, my recollection of this particular situation is that this was not money requested by the administration in any budget. It was money provided by the Congress. It was provided relatively late in the fiscal year.

Senator ANDREWS. Fine, but it's the law. If you come up in a hearing, whether you request it or don't request it, and the Congress writes it in because of testimony that's been developed, the money for building these buildings, these facilities, it then ceases to be a matter of whether the administration is interested or not interested.

If the administration is not interested in it, the administration should have sent up a deferral or a rescission. They did not. So you then assume they are going to go ahead and build it.

OBLIGATION OF CONSTRUCTION FUNDS

Mr. ITTEILAG. Senator, I believe it was our intent all along to proceed as quickly as possible under the circumstances. The point I was going to make was that there was little or no planning within the Department to utilize those funds until they were received.

Now, money was not deferred and in my judgment did not need to be deferred as long as we were proceeding as expeditiously as possible to use the funds in a wise and considered way. And my sense is that the Institute and Dr. Kupfer have done just that.

It certainly does not make any sense to try to obligate money before we are ready to use it wisely. It indeed has taken a long time, but we have too many examples of construction funds that have been awarded in an expeditious manner without a thoughtful process, and then later on having to deal with the problem of cost overruns.

I think it is preferable to do it in this sort of considered fashion in order that the money be used wisely.

Senator ANDREWS. Might I point out that you are guaranteeing a cost overrun when you drag your plans for 3 years. The thing that I'd like to know from the standpoint of the committee—because I obviously was not on this subcommittee at the point when the discussion developed as to the need for this money and the money was written into the law—is whether the delay was in the Institute or external to the Institute. Our clerk was here and he assures me there was a lot of discussion. It would be interesting for the committee to know the answer.

Doctor, were you held up by, shall we say, external forces?

Dr. KUPFER. Let me say two things, Senator. I think the Eye Institute moved as rapidly as possible because we recognized that this was considered a very high priority by the extramural community, and we wanted to be responsive to the Congress in providing these construction funds. However, I must say, there were some uncertainties concerning the fiscal year 1980 budget at that time, and the announcement that construction funds were available was delayed by the Office of the Director, NIH because of these uncertainties.

But I would say that in terms of the construction program, in terms of determining the manner by which these grants would be given, the need for matching funds, an assessment of what was most important in terms of construction—these activities did take time.

Now, perhaps it might be interesting if I just read you the timetable.

Senator ANDREWS. Sure.

IMPLEMENTATION OF CONSTRUCTION PROGRAM

Dr. KUPFER. When the funds were appropriated, we discussed with our National Advisory Eye Council what the guidelines should be. And I think this was absolutely essential because they are our advisory group and there were concerns about the need to have matching funds.

Senator ANDREWS. How long did that discussion take?

Dr. KUPFER. That was initiated in November 1979. The announcement was not issued until September 1980, in other words, almost 6 months later than planned. And during that time there was the preparation of the NEI guidelines and the announcement was prepared. There was some delay at that point. However, once that announcement was issued in September 1980, it took 18 months for the actual review and approval and granting of the construction funds. The funds were committed just recently, at the last Council.

So I think if we look at the 18-month period, one can feel confident that the speed with which these funds were committed was adequate.

Senator ANDREWS. Well, we understand from an inquiry we made that the NIH Director's office did not give NEI permission to release its announcement soliciting grant applications until August or September 1980——

Dr. KUPFER. Yes, sir.

Senator Andrews [continuing]. Because of the possible threat of deferring or rescinding this construction money.

And the ensuing 15 months has been spent processing and reviewing what Dr. Geller in his report characterized as a complicated application on a new type of project.

Dr. KUPFER. Yes.

FUNDS FOR CONSTRUCTION IN FISCAL YEAR 1982

Senator ANDREWS. And one of the reasons for examining this all is the fact that in the last bill we earmarked another $3 million from NEI money that's there. What type of a gestation period might we expect on that one? [Laughter.]

Dr. KUPFER. Well, sir, first, as I understand it, the continuing resolution directs us to take the lower of the House or Senate allowance for fiscal year 1982, and the House figure is the lower of the two. The House figure does not include, to the best of my knowledge, any construction funds. We have requested clarification of this point and are awaiting some decision concerning construction funds in this budget.

Senator ANDREWS. That's a new approach we are not aware of. My own thinking is that you are not allowed to zero-fund on those, but that was rather complicated, as you understand, the procedure we had between the House conferees and the Senate conferees.

It is a pretty close call because, in fact, you've got an electron microscope that you are splitting dollars with in here because the House figure for the National Eye Institute was indeed, as you just pointed out, less than the Senate figure. But the Senate figure was $133,014,000. The House figure was $132,920,000. And you are now telling us that you don't have the $3 million available for this because the House figure, which is the figure you take, the lesser of the two, is $94,000 under the Senate figure.

That strains my mathematical sensitivity, but if you could explain better why you have to drop 3 million dollars' worth of earmarking because of a $94,000 discrepancy in funding between the House and Senate bill, I'd be most intrigued.

Dr. KUPFER. Sir, we are holding these funds in reserve and are awaiting clarification and would welcome clarification on this point.

Senator ANDREWS. Well, speaking as only one member of the subcommittee, I think it's pretty clear when we come that close—you can take that out of pencils and wastepaper in a budget the size of yours. Certainly with a $94,000 discrepancy, you don't knock off $3 million in projects. And it's been 6 or 7 months while you have been trying to resolve that question, so it looks like the gestation period on this particular 3 million dollars' worth of building might be even longer than the last one.

And the question that needs asking now is: Why hasn't the subcommittee been notified of this question on your part if a decision has been made not to go along with the expressed direction of the subcommittee?

Dr. KUPFER. Again, to the best of my knowledge, these funds are being held pending clarification of this situation.

Senator ANDREWS. Well, where do you go for clarification?

Dr. KUPFER. Well, I believe we have gone through NIH channels to seek clarification on this point.

Senator ANDREWS. For 6 months?

Mr. ITTEILAG. Senator, could I comment on that?

Senator ANDREWS. Sure, I'd be glad to have you comment.

Mr. ITTEILAG. This matter has not been brought to my attention, but I suspect what the question is——

Senator ANDREWS. Well, where do they go for clarification if not through you?

FISCAL YEAR 1982 CONTINUING RESOLUTION

Mr. ITTEILAG. I would think they would go through the budget channels. But let me say it seems to me the issue is one of policy under the continuing resolution when an item is included in one House's bill and not included in the other House's bill. And under those circumstances, given the terms of the continuing resolution, the earmark would not stand.

Now, we would be more than willing to look at this from a legal point of view and have the General Counsel come to an expeditious conclusion on it because it seems to me it is an issue that needs to be decided from both the point of view of the Institute and of the committee. Further information on the use of NEI funding for facilities construction will be submitted to the committee at a later date.

Senator ANDREWS. Well, anything that would be expeditious at this point, of course, would be highly useful. But as I recall, not only the conference we had on this—and I was a conferee—but on the bill that we did complete in a subcommittee that I am chairman of, we had the usual procedure where we specifically included in the conference report the reference to any items that were put in by House or Senate. And we obviously deleted specifically the ones that weren't. And if we came up with a dollar figure that was adequate to cover them—we didn't knock out a $3 million item because of a $94,000 discrepancy.

And I would appreciate it and the subcommittee would appreciate it if you could provide a little bit more light on just exactly what's happening in this particular field.

Doctor, I didn't mean to spring that on you, but we are concerned. The subcommittee has felt that these are wise investments in the march against eye disease. That's the reason we put them in 3 years ago, 4 years ago, and that's the reason they were put in again. We do hope we can get the answers.

SUBMITTED QUESTIONS

I have some additional questions that I will give you to be answered for the record. I'd appreciate it if you'd provide those answers at the same time as you return the corrected hearing transcript.

Thank you very much.

Dr. KUPFER. Thank you, sir.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

GRANTS REDUCTION

Question: With a loss of 58 competing research grants between 1982 and 1983, what will this do to your effort to maintain a strong research base?

Answer: The reduction in research project grants that is being proposed in the 1983 budget will certainly slow the progress of ongoing research. A 21% decrease in the number of competing grants supported will allow minimal flexibility in pursuing promising new areas of research. Despite these limitations, the highest quality vision research could be maintained in 1983.

Reductions of this magnitude can probably be absorbed for a short time, but we would not be able to maintain a strong research base without stable Federal support for biomedical research in future years.

Question: What research in particular will be affected by the cutback?

Answer: A few examples of research that might be affected by the cutback are:

- studies to develop new animal models of eye diseases;
- clinical trials to develop better treatments for glaucoma; malignant eye tumors, and amblyopia;
- projects to develop improved drugs for recurrent corneal infections from herpes simplex virus;
- studies of effects of environmental factors on senile cataract, and
- research to characterize factors responsible for growth of abnormal retinal vessels.

Question: At a time when you are reducing investigator-initiated research, the real heart of NIH, why do you increase funding for Intramural Research and administrative expenditures?

Answer: The major portion of the increase included in the 1983 budget for intramural research, direct operations, and program management will be used for mandatory increases for items such as personnel compensation, telephone charges, and supplies and materials. The remainder will support investigator-initiated projects conducted by NEI intramural researchers and make it possible to fully support the new Laboratory of Molecular and Developmental Biology. This laboratory, which is an outgrowth of the NEI Section of Experimental Embryology, uses the powerful tools of recombinant DNA technology to analyze tissues of the eye at the gene level.

The gene-related studies of the LMDB add a new dimension to eye research in the NEI. Visual processes are being related to gene processes for the first time. These investigations are redefining the major components of the eye in terms of their genes and are paving the way for novel approaches to treatment of ophthalmic disorders, such as replacement of defective genes.

CLINICAL TRIALS

Question: Last year, plans for three additional clinical trials were mentioned: evaluating the benefits and risks of a laser procedure in treating glaucoma; studying malignant tumor of the eye; and determining the optimum age for surgery on crosseye or wall eye. What came of these plans?

Answer: Discussions have been held with investigators interested in pursuing these clinical trials. The plans for the glaucoma laser study have been modified by the investigators and a revised proposal is expected to be submitted shortly. The investigators interested in studying ocular melanoma are also modifying their project. We anticipate that they will resubmit their application in the summer of 1982. The ophthalmologists interested in surgery for crossed eyes are at a much earlier stage of development in their studies. They have held several meetings in order to determine specific objectives and methods and to develop a protocol. No specific time for submission of an application has been set.

Question: What results?

Answer: The studies have not progressed to a point that research results are available.

INTRAMURAL PROGRAM

Question: In its fiscal 1982 report, the Committee noted that a Laboratory of Molecular and Developmental Biology would be established in 1982 as part of your Intramural Program. What is the current status of the Laboratory, and what do you hope to gain from its work?

Answer: The Laboratory of Molecular and Developmental Biology (LMDB) was established on June 10, 1981.

The LMDB conducts research on the genetic basis of the visual system. The powerful tools of recombinant DNA technology are being used to analyze the eye at the gene level. The research is designed to further knowledge of both normal and pathogenic visual processes. The work includes investigations on developmental aspects of the eye so that we can better understand the foundation upon which the visual system is constructed and the causes of congenital and hereditary defects.

The gene-related studies of the LMDB add a new dimension to eye research in the NEI. Visual processes are being related to gene processes for the first time. These investigations are redefining the major components of the eye in terms of their genes and are paving the way for novel approaches to treatment of ophthalmic disorders, such as replacement of defective genes.

Question: How much will it cost in 1982 and 1983?

Answer: The estimated cost for FY 1982 is $615,000 and for FY 1983, $650,000.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: The NEI is undertaking several approaches to effecting administrative cost savings. In FY 1983, the Office of Program Planning, Analysis, and Evaluation will complete the design and implementation of a new computer system to maintain and query the extramural data bases. This system will allow NEI personnel to obtain information about grants and contracts much more quickly and effectively than under current procedures, thereby improving managerial decision-making and efficiency and lessening the amount of staff time needed to respond to program inquiries.

The Program Analysis Section will also undertake an inhouse study to determine the Institute-wide data processing and word processing needs for equipment and services. An evaluation will then be made and recommendations proposed for developing a unified system for the entire Institute. These measures are expected to facilitate communication from one component of the Institute to another, reduce staff time, and decrease dependence on paperwork.

In addition to the above, the NEI is also sponsoring a series of grant clinics aimed at improving the efficiency of the grant application, review, and management process. At these clinics, Institute staff provide a detailed explanation of grant policies, rules, regulations and legal responsibilities. Sharing this type of information is expected to reduce the amount of time ordinarily spent on handling inquiries about grant application procedures, processing the applications, and managing the grants program. The result is a reduction in the paperwork burden, and a savings in indirect costs, supplies, and staff time.

ADMINISTRATIVE PRIORITIES

Question: What are your most important administrative concerns --and what are your least important concerns?

Answer: A high priority for the National Eye Institute research program is the establishment of the Laboratory of Molecular and Developmental Biology. Research on the genetic bases of normal and abnormal processes in the visual system is believed to hold the key for future scientific breakthroughs in treating and preventing eye diseases and visual disorders.

The Ambulatory Care Research Facility (ACRF) was designed to complement the NIH Clinical Center by providing a unique facility for laboratory and clinical research. Another important administrative concern is that the programs relocated to the ACRF will have the resources required to effect optimal use of this new ACRF space. When those laboratories are fully operational, there will be further opportunity for collaborative studies among basic researchers and clinicians, which will hopefully result in quick and efficient translation of research results into clinical situations.

Question: What criteria do you use for determining your administrative priorities?

Answer: Fulfillment of the Institute's mission depends on the effective communication of its research accomplishments, goals and programs--to the general public, to health care providers, and to vision researchers. To accomplish this mission in light of current budget constraints, Institute officials are setting priorities, program by program, based on potential benefits: effectiveness, cost and time savings, efficiency and economies of scale and are prepared to not carry out those that do not meet the criteria.

NEI RESEARCH PRIORITIES

Question: What percentage of the grants funded by NEI in FY 1981 were in areas considered by the National Advisory Eye Council to be of high program relevance and priority?

Answer: We estimate that more than 50 percent of NEI grants funded in FY 1981 were in the Council's high priority areas as defined in the 1978-1982 national vision research plan. For the forthcoming Vision Research--A National Plan: 1983-1987 we will be tracking funded grants as well as unfunded applications for these years in two categories: "Program Development Priorities," and "Program Base." Program Development Priorities are defined as those research areas in which a significant number of additional grants are judged to be needed throughout the planning period. The Program Base is defined as those portions of the program considered to be adequately funded already and for which only modest growth, maintenance, or reduction, is projected. These two categories were established in an effort to be more selective about what areas of vision research are defined as NEI program priorities.

Using this more restrictive definition, our analysis shows that approximately 30 percent of the grants funded in FY 1981 are in areas newly designated as Program Development Priorities. The remaining 70 percent of grants are in areas that constitute the Program Base. Applications for research grants in these Program Base areas considered by the study sections to have high scientific merit will continue to be funded.

Question: What are some of the priorities the Council has established?

Answer: The following is a summary list of priorities which will appear in the first volume of the forthcoming national plan.

NEI PROGRAM DEVELOPMENT PRIORITIES FY 1983-1987

Retinal and Choroidal Diseases

- Exploiting the new experimental capabilities provided by technological advances in the areas of molecular biology, microelectrode fabrication, and tissue culture in basic research on (human) retinal cells and tissues.

- Assessing new pharmacological and immunological approaches to the management and prevention of uveitis.

- Developing and applying better noninvasive tests of retinal visual and vascular functions in normal and pathological conditions.

- Applying the powerful new methods of molecular biology (e.g., techniques of gene splicing, gene cloning, and gene transplantation) in studies of human retinitis pigmentosa and allied diseases and animals with hereditary retinal degenerations.

- Expanding studies of the metabolic interrelationships among the retina, the retinal pigment epithelium, and the choroid. Special emphasis would be placed on the effects of age, light, drugs and antioxidants.

- Assessing the damaging effects of environmental, nutritional, and drug-related factors on retinal function and developing screening systems for ophthalmic toxicity, including *in vivo* physiologic tests and *in vitro* tests, using cultured ocular tissue.

- Characterizing the retinal neurotransmitter substances, the associated metabolic pathways, and the effects of neurotransmitters of postsynaptic cells, with the aim of developing rational pharmacological therapies for retinal neural disorders.

- Pursuing new investigations of the basic biology and management of sight and life-threatening intraocular tumors.

Corneal Diseases

- Determining the neuronal and viral factors contributing to herpetic latency; with disease state, determining viral latency patterns and mechanisms which trigger viral reactivation and shedding.

- Developing specific antiviral drugs for acute and recurrent corneal infection.

- Developing methods to stimulate repair of corneal endothelium, *in vivo*, especially in primates.

- Studying biological effects of existing and proposed procedures and materials for surgical or lens correction of refractive error.

- o Studying epithelial defect formation, occurrence, and persistence, and relationship with neural supply.

- o Studying the differential effects of various kinds of steroids and other agents with regard to differential effects on tissue destruction and wound healing.

Cataract

- o Studying changes in cell membrane and cytoskeletal structures in human cataracts.

- o Determining cataract risk factors through epidemiological studies.

- o Developing and testing promising anti-cataract drugs, for example, aldose reductase inhibitors that may delay formation of diabetic cataract and perhaps the development of other diabetic ocular complications as well.

- o Studying genetic lesions in hereditary and congenital human cataracts.

- o Studying the possible cataractogenic effects of radiation: ionizing, microwave, and ultraviolet.

- o Studying various methods of aphakic correction following cataract surgery.

Glaucoma

- o Developing improved methods of detection, diagnosis, and drug and surgical treatments for glaucoma.

- o Conducting clinical and laboratory studies to define risk factors (genetic, racial, and environmental) for the development of damage to the optic nerve in glaucoma and the reasons for the varying susceptibilities to optic nerve damage.

- o Devising new noninvasive clinical techniques for studies of aqueous humor formation and flow, for continuous monitoring of intraocular pressure, and for the study of optic nerve damage in glaucoma.

- o Exploiting new experimental methods to study the basic physiology and pharmacology of fluid movement in the eye and the control of aqueous humor inflow in man and in primates.

- o Studying the cell biology and molecular characteristics of outflow tissues and their abnormalities in glaucoma, especially using tissue and organ culture techniques.

- o Investigating the mechanisms of glaucoma secondary to the formation of abnormal blood vessels on the iris and methods for its treatment.

- o Establishing eye donor programs so that appropriately obtained and preserved human tissues from well-characterized glaucoma patients will become available for correlations between clinical history and tissue damage and for cell biology studies.

Strabismus, Amblyopia, and Visual Processing

- Developing improved surgical, pharmacological, and other treatments for strabismus; employing controlled trials to evaluate the most promising treatment, and determining how the timing of treatment influences its success.
- Developing and evaluating new treatments for amblyopia; including masking regimens, contact lenses, or pharmacological approaches.
- Exploring factors that may play a role in permitting regeneration of the optic nerve.
- Devising noninvasive methods for studying the development of the visual systems of human infants, particularly methods that could be used in the clinic for diagnosing and monitoring the effects of treatment.
- Studying the anatomy, physiology, and behavior of the systems that are important in vergence. Vergence is movement of the two eyes toward or away from each other to allow focus on a nearby or faraway object. Accommodation is changing of the shape of the lens to allow the eye to focus on an object in normally developing infants as well as in those at risk for strabismus.
- Studying the normal development of the eye movement system and the disorders that may affect it. Techniques to record eye movements quantitatively in newborns and young children are especially needed.
- Investigating the structure, function, and development of the visual system at the molecular level including studies of cellular receptor sites, cell specificity, neurotransmitters and peptides, and immunological approaches.
- Determining the causes of and mechanisms for the development of myopia in humans including expanded studies with animal models and relating the results of animal studies to the human condition.

Low Vision and Rehabilitation

- Studying visual characteristics of individuals with visual impairments.
- Developing an improved taxonomy of visual impairment that includes specification of associated disabilities.

- Conducting epidemiological studies of visual impairment.
- Conducting research on optical, electronic, and other rehabilitative needs of visually impaired persons.
- Developing special contact lenses and aids for patients with anterior segment problems.
- Conducting research on basic skills relating to mobility and orientation.
- Encouraging "human engineering" studies of the needs of the visually impaired population.
- Developing experimental designs applicable to the study of small samples of the visually impaired population.
- Studying the effects of prior visual experience upon the nature and extent of visual impairment in young children.
- Studying special problems or adaptations required in response to visual impairment in the older population.

PREVENTION OF DISEASE

Question: You indicate there is no way of preventing such diseases of the eye as diabetic retinopathy--and macular degeneration which afflicts the elderly. Are you working on finding a means of prevention--or is this out of the question?

Answer: The prevention of these two leading causes of blindness and disability is a major objective of the National Eye Institute's program. The forthcoming new national vision research plan for the years 1983-1987 stresses the importance of research on the prevention of diabetic retinopathy and macular degeneration while at the same time calling for improved methods of treating these disorders until such means can be found.

For diabetic retinopathy, various approaches to prevention are being explored. One is the new Early Treatment Diabetic Retinopathy Study, which, although it is not aimed at preventing the onset of this condition, is directed at preventing the disease's progression to advanced stages where sight is threatened. Since the early stages of diabetic retinopathy frequently do not cause loss of sight, early laser treatment, if found effective, would for all practical purposes be a means of prevention. Other studies are aimed at preventing the onset of diabetic retinopathy itself. In one study, the objective is to find out if better control of the patient's diabetes can prevent or forestall retinopathy. Another approach is to test whether drugs that act by inhibiting the enzyme aldose reductase, believed to play a role in initiating diabetic retinopathy, can prevent or delay the onset of this disease. The fouth major approach to prevention is the study of risk factors for diabetic retinopathy. This appears to be an area ripe for investigation since many diabetics show no signs of retinopathy even after having the disease for several years.

In the case of macular degeneration, much more needs to be learned about the pathologic mechanisms underlying this disease before we can hope to prevent it, particularly since it is very closely linked to the general aging process. Effective means of treating macular degeneration are also lacking, although laser treatment may be helpful in certain types and stages of the disease. To determine whether laser treatment is of value in preventing loss of visual function in people with senile macular degeneration, the NEI is supporting a multicenter clinical trial, the Macular Photocoagulation Study. Emphasis is also being given to epidemiologic studies of macular degeneration due to exposure, diet, occupation, ethnic differences, and contributing systemic abnormalities. In addition, the development of noninvasive diagnostic techniques is being encouraged to improve early detection of macular degeneration and to provide a basis for assessing whatever therapeutic and preventive measures are developed. Other approaches include the study of blood flow in the retina and how aging-related changes may selectively damage the macula while leaving the rest of the retina intact.

MAJOR STUDIES UNDERWAY

Question: You have at least two major studies under way: the Retinal Branch Vein Occlusion Study, and the Early Treatment Diabetic Retinopathy Study. How extensive are these studies -- what do you hope to show?

Answer: Retinal branch vein occlusion is the second most common retinal vascular disease after diabetic retinopathy. Many treatments for this disorder have been attempted over the past several years, but none has proven effective. At present, the only treatment which seems at all promising in preventing visual loss from branch vein occlusion is laser photocoagulation.

The Branch Vein Occlusion Clinical Research Study, with the support of the National Eye Institute, will determine whether or not laser photocoagulation therapy is effective in preventing loss of sight due to this devastating disorder of the eye. More than 500 patients with various stages of retinal branch vein occlusion have been enrolled in the study during the past three years. These patients are being followed at five cooperating eye-research centers across the United States: Wilmer Ophthalmological Institute at Johns Hopkins University Hospital, Bascom Palmer Eye Institute at the University of Miami, Estelle Doheney Eye Foundation at the University of Southern California, Eye Research Institute of the Retina Foundation in Boston, and Illinois Eye and Ear Infirmary at the University of Illinois Medical Center in Chicago. The National Eye Institute projects that initial results with respect to the efficacy and safety of laser photocoagulation therapy in preventing complications early in the disease process may be available as early as 1983.

The Early Treatment Diabetic Retinopathy Study (ETDRS) is an outgrowth of the Diabetic Retinopathy Study which showed that photocoagulation can substantially reduce the risk of blindness in people with advanced diabetic retinopathy. This common complication of diabetes is the leading cause of blindness among adults.

In the ETDRS, investigators at 19 clinics throughout the country are trying to determine whether photocogulation can be even more effective in preventing blindness if patients are treated earlier in the course of their disease than the patients in the first study. In addition, the ETDRS will test the effects of photocoagulation on macular edema, a condition which often accompanies diabetic retinopathy, and investigate aspirin's ability to slow down the disease process.

Question: How many people are involved -- and what will the cost be in fiscal 1982 and 1983?

Answer: The annual cost of the Branch Vein Occlusion study is approximately $500,000 in 1982 and 1983 and approximately 500 patients have been enrolled.

Approximately 4,000 patients are being recruited for the ETDRS study. Following treatment, follow-up examinations will be conducted at 4-month intervals for at least five years.

The estimated cost of the ETDRS is $3,800,000 in 1982 and $4,200,000 in 1983.

MARIJUANA FOR GLAUCOMA

Question: Please explain the NEI's position on the use of marijuana to treat glaucoma.

Answer: Over 2 years ago the NEI published an announcement indicating our interest in research proposals dealing with cannabinoids in the treatment of glaucoma: NIH Guide for Contracts, Vol. 7, No. 18, Nov. 27, 1978. Our interest in this subject has not changed, i.e., we hope to stimulate research aimed at:

- determining if cannabinoids, defined as marijuana, its components or derivatives, can effectively and safely lower intraocular pressure in different types of glaucoma.
- finding out if use of cannabinoids in treating glaucoma is accompanied by the deleterious side effects, such as diminished blood supply to the optic nerve which worsens the glaucoma; a precipitous fall in blood pressure and fainting; undesirable psychologic or behavioral effects.
- determining if prolonged use of cannabinoids reduces their efficacy in lowering intraocular pressure, as is the case with commonly used anti-glaucoma medications, and if cannabinoids are compatible with other drugs used to treat glaucoma.
- determining if cannabinoids act to reduce intraocular pressure at different tissue sites or by other mechanisms than do drugs commonly used to treat glaucoma. If they do act in the same way as another drug there would be little reason to add them to present means of treating glaucoma.
- conducting basic research on the physiologic and pharmacologic effects of cannabinoids, using experimental animals and isolated

tissues and cells grown in the laboratory. The dual objectives would be to learn which processes in the eye are affected and to use this knowledge to design and test improved anti-glaucoma drugs.

It should be noted that drugs or combinations of drugs presently approved for use in glaucoma patients are successful in treating the great majority of patients with open-angle glaucoma, and that surgery increases the percentage of patients whose disease can be controlled by existing therapy. A new drug should exhibit significant advantages over drugs in current use, the most important of which would be to control cases of glaucoma intractable to other types of therapy. To determine if cannabinoids meet this requirement is an important objective of NEI-supported research on possible therapeutic applications of cannabinoids.

Question: What authority do you have for using marijuana in the treatment of glaucoma?

Answer: The NEI encourages scientists to submit grant applications for projects to answer the basic questions about cannabinoids posed above. Successful applicants must receive approval to use marijuana from the Food and Drug Administration, approval and cannabinoids from the National Institute of Drug Abuse, and clearance from the Drug Enforcement Agency.

MAN-MADE DRUGS

Question: Aren't there man-made drugs that can be effective?

Answer: Yes. Drugs of several major classes are now used to treat glaucoma: miotics (like pilocarpine) which improve outflow of aqueous humor; adrenergics (like epinephrine) which diminish inflow and improve aqueous humor outflow; and beta-blockers (like timolol) and carbonic anhydrase inhibitors (like Diamox), both of which diminish the inflow of aqueous humor. Drugs of these different classes are also useful in combination since they act in different ways to control the level of intraocular pressure, which is maintained by balancing fluid inflow against the outflow.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

STATEMENT OF DR. DAVID P. RALL, DIRECTOR

ACCOMPANIED BY:

DR. THOMAS P. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

PAUL G. WAUGAMAN, EXECUTIVE OFFICER

ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator ANDREWS. Our next witness is Dr. David P. Rall, Director of the National Institute of Environmental Health Sciences. NIEHS is located at Research Triangle Park in North Carolina. It's the only Institute of NIH not located in the Washington area. I'm sure your colleagues think you are blessed with a lot better weather than we here have been getting in the last couple or 3 months. In fact, Washington weather is almost bordering on North Dakota weather. It was colder yesterday in Washington, if you can imagine, than out in the State of North Dakota.

We welcome you to the committee. We'd appreciate it if you'd introduce your colleagues and, of course, summarize your opening statement, if you could, so we could have more time for questions.

INTRODUCTION OF ASSOCIATES

Dr. RALL. Yes, indeed. Thank you very much, Senator Andrews. It is a pleasure to come up North to testify occasionally.

I'd like to introduce on my left Mr. Paul Waugaman, our Executive Officer, and Mr. Jack Rigsby, our new Budget Officer.

You noted appropriately that we are the only Institute located outside the Bethesda campus. I am pleased that this spring we moved into the office portion of our new permanent facility in Research Triangle Park, N.C.

Senator ANDREWS. Not only are you removed by distance, but you are the Institute that got the highest percentage increase. Of course, there is a unique reason for that.

Dr. RALL. Oh, yes; we'll go into that later on. [Laughter.]

OPENING STATEMENT HIGHLIGHTS

Senator ANDREWS. I don't know whether it's proximity or distance makes the heart grow fonder.

Dr. RALL. It's bookkeeping. [Laughter.]

But seriously, we lived for 16 years in North Carolina in rented temporary laboratory and office space, and it meant very much to me and our scientists to be able to begin to move into a permanent federally owned building on federally owned land, and we appreciate the support of the committee in providing that support.

The apparent increase in our budget is due to the transfer—on the recommendation of the Director of the Cancer Institute, Dr. DeVita, and the former Director of NIH, Dr. Fredrickson—of the NCI bioassay program, funded at almost $50 million, to NIEHS. This now gives us in one Institute an opportunity to move from basic research through applied research, to actual testing of chemicals for a whole variety of toxic effects.

Now, one of our major programs is in testing chemicals for mutagenic activity or looking for mutagens. Mutagens are chemicals that damage DNA, the substance that is involved in the transmission of information, genetic information, from one form and function, from parent to offspring, and mutations can cause genetic disease, birth defects, or cancer.

Our intramural scientists and our grantees are working very diligently on the mechanism of mutations, how chemicals affect the DNA. Interestingly, it was 31 years ago that research which showed that genes can "jump" was done at the Cold Spring Harbor Laboratories. It is now apparent that some of these "jumping genes" tend to be very much more susceptible to chemical mutagens than normal genes. This is very exciting and useful basic research.

Now, at the other end of the spectrum, we have the only program in the world for testing chemicals for mutagenic activity with careful and adequate controls which assure accurate, consistent, and reproducible results. I think this illustrates the breadth of NIEHS's efforts.

I would like to make some more comments before we move into the question period.

We talk often about how many chemicals are carcinogens; and if you give a mouse enough of anything it will cause a carcinogenic effect. We have reported this year on five different food additives, called gums, which we consume really in fairly significant amounts. We have studied them very thoroughly, and they are not carcinogenic, they do not have other significant toxic effects.

Now, I think this is very reassuring and should be assuring to the consumer.

Finally, we did find one unusual compound, a plasticizer called diethylhexylphthalate. It is responsible for the "new car" smell you get when you are fortunate enough to buy a new car. We believe we have uncovered toxic effects in a whole series of compounds like diethylhexylphthalate, which previously had been thought not to be toxic at all.

So I thank you and I would be delighted to answer questions.

PREPARED STATEMENT

Senator ANDREWS. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. DAVID P. RALL

Mr. Chairman and Members of the Committee, it is a pleasure to be with you today to tell you about some of the things that are going on at the National Institute of Environmental Health Sciences.

One event at our Institute that is very exciting is the move into our new 260,000 square foot building in Research Triangle Park, North Carolina. We have occupied two of the building's five wings. These two wings contain the offices of the Health Hazard Assessment, Toxicology Research and Testing, and Biometry and Risk Assessment programs, administrative activities, our computer facility, the cafeteria and an auditorium for scientific conferences. The three other wings, which we expect to begin occupying this year, will contain state-of-the-art biomedical research laboratories designed to accommodate safely the most sophisticated experiments in chemical toxicology, genetics, microbiology, and biophysics. Elaborate and sophisticated air handling, waste disposal and utility distribution systems combine to provide sites in which experiments can be done safely and with little chance of cross-contamination.

The importance of this building is that the Government's facilities for studying environmental health problems will be as modern as those anywhere in the world. But the move is also important for another reason: for the first time in NIEHS' 16-year history we are operating out of Government-owned space. I think that this fact has significant symbolic importance--it creates a sense of permanence and stability, as well as providing more current technology for our scientists.

At NIEHS we bring together scientists from many related fields to conduct both basic and applied research aimed at understanding and preventing environmentally-caused health effects such as pulmonary and kidney diseases, cancer, birth defects, immune system dysfunction, and so forth. We conduct this research both in-house and through grants and contracts. We also support the training of the expanding cadre of highly-trained professionals needed to meet the challenge of understanding the relationship between environmental agents and human health.

Our research is aimed at solving such problems as:

- What agents are toxic and at what doses;
- How they interact and move through the environment;
- How these agents are altered by the human body to become more or less toxic;
- How they damage the human genetic structure; the immune, endocrine, or nervous systems; reproductive functioning, or organs such as the kidneys, liver and lungs;

- What effects are caused by long-term, low-level exposure to different toxic agents in combination, the kinds of exposures each of us faces in the real world.

At NIEHS we conduct both applied research on such practical problems as devising faster and less expensive tests to identify toxic agents and basic research such as that in genetics which seeks to understand the underlying mechanisms of toxicity, find specific biological markers in the body, and trace the path from exposure to disease. In our research we observe effects in cell cultures and in laboratory animals, by employing epidemiological techniques to look at large human populations and by using mathematical models in computers.

Some of this research is immediately applicable in the fight to prevent disease. When we identify a chemical that can cause toxic effects such as cancer in animals and to which many of us are exposed, this finding can help focus attention on estimating dose-response relationships and evaluating human risk. It can also lead to changes in manufacturing processes to protect workers and the public and it may lead to regulatory action. Other research, such as that with recombinant DNA, seeks to unravel the mysteries of life and explores regions along the thin edge between the known and the unknown.

As I will discuss in a little while, in science sometimes decades may elapse before the various parts of the puzzle fit together. The ultimate goal of all health research, both basic and applied, is to develop additional knowledge that can help prevent or reduce the pain and suffering--and the economic costs--due to environmentally-induced diseases.

This last year we have reorganized NIEHS to more accurately reflect what is actually done in each specific NIEHS program. These are the Biometry and Risk Assessment Program (BRAP), the Extramural Program (EP), the Intramural Research Program (IRP), and the Toxicology Research and Testing Program (TRTP). I would like to give you examples of some of the research being done by each of these Programs.

In 1951, when Dr. Barbara McClintock at the Cold Spring Harbor Laboratories explained her experiments on genetic control in corn, her discovery was met with apparent disbelief. Genes were assumed to be the stable elements of chromosomes. Her notion of "transposable" genetic elements--"jumping genes" if you will--was not taken seriously. In the 31 years since Dr. McClintock first described her discovery, the science of genetics has come a long way. Her hypothesis of the "jumping genes" could not be substantiated until we could manipulate nucleic acids. Although we do not yet know exactly how these "jumping genes" function at the molecular level, NIEHS intramural scientists recently have found that in Drosophila--fruit flies--if a particular "transposable" gene, or DNA element, is inserted into a chromosome, the rate of genetic mutation increases greatly.

This discovery is one of many other advances made in the past decade. This surge of new knowledge about genetics which has grown up around recombinant DNA technology, gene cloning, and DNA sequencing will have a profound effect on our understanding of how environmental chemicals cause disease in those exposed or in their children. Many cancers are believed to be produced by mutation in somatic cells, that is, cells other than the sperm or egg. Injury to our germ cells, however, can cause birth defects and developmental disorders. We do not know precisely what percentage of either cancer or heritable genetic disease is related to environmental chemicals, but we believe this to be significant and often preventable.

The NIEHS Intramural programs in genetics concentrate on understanding how mutations can cause disease in our children. The results of this research can be used to estimate the risks to man from exposures to chemicals in the environment with greater precision than is now possible.

Although they are of considerable value, current methods of estimating human risk on the basis of evidence obtained from animal tests are empirical yet considerably valuable. Greater understanding of the fundamental mechanisms by which environmental chemicals inflict injury promises to provide a more scientific basis for these estimates.

A large part of the NIEHS effort in applied toxicology research is conducted by the Toxicology Research and Testing Program, which constitutes a major portion of the National Toxicology Program (NTP). TRTP was created in 1981 to merge the Bioassay Testing Program transferred from the National Cancer Institute with NIEHS' toxicology test development efforts. TRTP has two related roles: first, conventional methods are used to test chemicals of public health concern and second, newer, faster, and less expensive methods are being developed to determine whether given chemicals might be hazardous.

One frequently hears people say that, "Oh, everything causes cancer, so what's the use?" But the statement is not true. It is a misconception--a widespread one, I am afraid--that every time we test a substance in animals it causes cancer. This perception is wrongly held. First, people tend to remember--and the press tends to report--only the most spectacular findings. Stories about chemicals that are safe are no more newsworthy than stories about airplanes that fly safely. And, second, many of these chemicals are tested because there is some suspicion about them to begin with. The results show that in the NCI-NTP cancer bioassay tests using rodents, less than half the chemicals tested turn out to be positive, that is, cause cancer in animals. And please remember, as I said, these chemicals were tested because someone thought they might actually be potentially hazardous. Actually, scientists have little idea how many of the 40,000-60,000 chemicals in commerce are in fact hazardous. We guess a small percentage. For this reason, the NTP Agencies are having the National Academy of Sciences look at the universe of chemicals to which people are exposed and attempt to determine which have been tested and which need testing.

The NIH portion of NTP, TRTP, has completed some interesting studies this year. For example, we have reported on five gums. All but one are used in large amounts in foods such as bakery and confectionary goods; meat, fish and dairy products; cereals and processed foods; and as emulsifiers, thickening agents, or stabilizers. These substances, which have never been carefully tested before--Agar, Guar Gum, Gum Arabic, Locust Bean Gum and Tara Gum--are all negative in recent NCI/NTP carcinogenesis bioassays. That is, as far as we can tell, they do not cause cancer in animals and, therefore, do not represent a hazard to humans. That is good news, especially in view of the widespread exposure.

Mannitol--another substance in food, which is also used medically and occurs naturally in onions, celery, strawberries and cocoa beans--was also negative in our tests. And that is good news too, again because of the heavy human consumption.

I have often discussed with you how really dangerous inhaled asbestos is. Many World War II shipyard workers face death by cancer because of exposures inside ships 40 years ago. Even a few months of working with asbestos, or of living in the same house with someone who did, can lead to cancer. This situation can only be described as tragic. Knowing what a deadly substance asbestos is when inhaled, there has been great concern about the population drinking or ingesting asbestos fibers either because their water supply is contaminated naturally or from ore mining operations--such as near Lake Superior, Seattle, or San Francisco--or because water is carried through asbestos-lined pipes. When water supplies in 365 cities were analyzed, detectable asbestos was found in 45 percent.

NTP is in the process of evaluating the risk from ingested asbestos. The good news is that the first two studies being conducted by NTP, chrysotile and amosite asbestos administered orally to hamsters, indicate that these do not cause cancer. Other studies are nearing completion.

I would not want to leave the impression that NTP results are always so encouraging. One result was unexpected and is quite worrisome. That is our finding that Di(2-ethylhexyl)phthalate (DEHP), which is used to make PVC plastics more flexible, causes cancer in animals. This is of concern because DEHP is found in plasma stored in hospital blood bags and that kidney patients on dialysis, especially children, receive considerable levels of DEHP. So there is some unknown risk involved here.

The NIEHS Extramural Program is funding an important study of the health effects of both indoor and outdoor air pollution on the health of children and adults. Researchers at the Harvard School of Public Health are studying six cities, each with a different mix of air pollutants. For example, one city has virtually clean air, one city has a heavy concentration of sulfates but no nitrates, another is heavy in nitrates and has few sulfates, and so on. We are looking at the health records of a random sample of children and adults to determine whether there is a correlation between particular types and levels of air pollution and specific health effects.

As I mentioned, the study is not only looking at the effects of the air we breathe outdoors, but that indoors--where we spend most of our time--as well. The investigators are interested in the effects of such substances as cigarette smoke and gas stove emissions.

This is the seventh year of data collection. In the course of the investigation, there has been a marked improvement in data collection and air monitoring capabilities. To date, although a small pulmonary effect has been detected in Steubenville, Ohio, one city being studied, investigators have so far been unable to identify a specific effect that can be causally related to a particular type and concentration of pollution.

In closing, I will mention one other NIEHS project. That is BRAP's study of 900 North Carolina mothers and their babies. We are measuring levels of PCBs and other chemicals in mothers' milk to determine what effect, if any, this exposure may have on their babies' health. This is a long-term study, possibly tracking the participants until the babies are of school age. The large amounts of data obtained are currently being analyzed. We will keep the Committee informed of results as they become available. These are just some of the many things going on at NIEHS.

Our budget request for fiscal year 1983 is $157,448,000, an increase of $3,190,000 over the comparable 1982 level. I would be happy to answer your questions.

BIOGRAPHICAL SKETCH

David Platt Rall

Birthplace and Date:	Aurora, Illinois; August 3, 1926
Marital Status:	Married; two children
Education:	Public Schools, Naperville, Illinois B.S., North Central College, Naperville (1946) M.S. (Pharmacology), Northwestern University (1948) Ph.D. (Pharmacology), Northwestern University (1951) M.D., Northwestern University School of Medicine (1951)
Professional Training:	Internship; Second (Cornell) Medical Division Bellevue Hospital, 1952-53
Experience:	Director, National Institute of Environmental Health Sciences, NIH, 1971-present Director, National Toxicology Program, November 1978 to present Assistant Surgeon General, USPHS, 1971-present Associate Scientific Director for Experimental Therapeutics, National Cancer Institute, 1966-71 Medical Director, USPHS, 1963-71 Chief, Laboratory of Chemical Pharmacology, National Cancer Institute, 1963-69 Senior Surgeon, USPHS, 1959-69 Head, Clinical Pharmacology and Experimental Therapeutics Service, General Medicine Branch, National Cancer Institute, 1958-63 Surgeon, USPHS, 1955-59 Scientist, Laboratory of Chemical Pharmacology, National Cancer Institute, 1953-55 Research Associate in Pharmacology, Northwestern University, 1950 Assistant in Pharmacology, Northwestern University 1949-50 Baxter Fellow in Pharmacology, Northwestern University, 1947-49
Association Memberships:	American Association for the Advancement of Science American Association for Cancer Research American College of Preventive Medicine American Public Health Association American Society for Clinical Investigation American Society for Pharmacology and Experimental Therapeutics Federation of American Societies for Experimental Biology Society for Occupational and Environmental Health Society for Risk Analysis Society of Toxicology
Honors and Other Special Scientific Recognition:	Head, DHHS Delegation, US/Japan Non-Energy R&D Cooperative Agreement Joint Committee Meeting, Tokyo, Japan, September 1981 Chairman, WHO Programme Advisory Committee, 1980-81 Member, WHO Programme Advisory Committee, 1980-present

Member, Institute of Medicine, National Academy of Sciences, 1979
Nellie Fox Lecturer, Northwestern University Medical School, April 1978
Chairman, Committee on Health and Environmental Effects of Increased Coal Utilization, 1977-78
Harrington Lecturer, University of Buffalo, April 1976
Member, NAS Safe Drinking Water Committee, 1975-1977
Member, Secretary's Review Panel on New Drug Regulation, 1975-76
Associate Editor, Journal of Toxicology and Environmental Health, 1974-78
Editorial Board, Archives of Environmental Health, 1973-76
Chairman, DHHS Committee to Coordinate Environmental and Related Programs, 1973-present
Chairman, Subcommittee on Environmental and Occupational Health, Joint Working Group on Health Cooperation, US/Egypt Cooperative Agreement, 1972-present
US Coordinator, Environmental Health Program, US-USSR Health Exchange Agreement, 1972-present
US Coordinator, Biological and Genetic Consequences Project, US-USSR Environmental Protection Agreement, 1972-present
US Coordinator, US-UK Cooperative Program in Environmental Health Sciences, 1972
Adjunct Professor, University of North Carolina, Chapel Hill, 1972-present
Chairman, OST-CEQ Ad Hoc Committee on Environmental Health Research, 1971-72
Associate Editor, Cancer Research, 1970-74
Chairman, HEW Departmental Committee on Drug Research and Regulations, 1970
Editorial Board, Pharmacological Reviews, 1969-72
Chairman, National Institute of General Medical Science
Member, National Institutes of Health Chemotherapy Study Section, 1965-67
Editorial Board, Proceedings of the Society for Experimental Biology and Medicine, 1962-65
Lecturer in Physiology, Medical School, George Washington University, 1958-62
PHS Meritorious Service Medal, 1966
DHEW Distinguished Service Medal, April 1975

Research Interests: Dr. Rall has authored and co-authored approximately 150 published papers relating to comparative pharmacology, cancer chemotherapy, blood-brain barrier, blood CSF barrier, pesticide toxicology, and drug research and regulation.

RESEARCH AND TRAINING EFFORTS

Senator Andrews. Thank you very much, Doctor.

As I have asked your colleagues, the budget proposes to cap indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent, and to maintain training allowances of slightly below the fiscal 1982 level.

What are these policies going to do to your research and training efforts, and what will they do to the ability of grant recipients to produce good science and good research?

Dr. Rall. Well, they certainly will cause some belt-tightening and some slowdown in the research effort; there's just no question about that. But let me describe a little more fully what will happen.

We will negotiate with each grantee to try to get the reduction as equitable as possible, taking into account the importance of the work in progress, and other issues.

This will slow down the efforts of the grantees with whom we are dealing.

I would point out, however, two things: One, the dollar savings to our budget will allow us to fund 16 grants which we would otherwise not have been able to fund. That is, most of our grantees will have to pull in their belts a little bit so that 16 scientists can have grants to do their work. It is a trade-off that, given the very limited budget, we thought was appropriate.

And although we have negotiated down an average of 4 percent, this year the average grant's dollar size still increases 6 percent from one year to the next.

It is a belt-tightening exercise, and it is not pleasant but it seems necessary.

NCI BIOASSAY TRANSFER

Senator ANDREWS. Doctor, the budget indicates that your Institute will get a $51 million increase in fiscal 1982, with most of this coming from the transfer of activities relating to testing chemical compounds from the National Cancer Institute to you.

Can you tell us a little more about this. How many people will you get from NCI and where will they be housed?

Dr. RALL. This is related to the development of the national toxicology program, which began in November 1978. NTP was an attempt to coordinate and better focus the toxicology test development and test validation efforts within the Department.

There were efforts going on in the National Center for Toxicological Research in Pine Bluff, Ark.; the National Institute for Occupational Safety and Health, primarily in Cincinnati, Ohio; at our Institute in North Carolina where we were doing about 15 million dollars' worth of testing and test development; and at the Cancer Institute which had the bulk of the testing effort, but it was focused only on looking for cancer, only on the single point of a "yes or no" carcinogenesis assay.

We pooled these efforts under the national toxicology program. I was appointed director. From that beginning, NIEHS and NCI worked together very, very closely trying to broaden the NCI tests so you'd look for neurological disease, kidney disease, and so forth, in addition to cancer.

As we worked closely, it became apparent it was very hard to have a large coordinated program that reported to two Institute Directors. This offered a great opportunity for confusion.

Dr. DeVita and Dr. Fredrickson suggested that it would be more appropriate to transfer the cancer bioassay program to NIEHS since we were concerned about all the effects of chemicals, including cancer, and because we would have, with the opening up of our new facility, laboratory space that would allow some of the scientists in the cancer bioassay program to do laboratory research. Secretary Schweiker approved the transfer last summer.

Now, in terms of transferring people, there were about 95 positions involved. About 35 employees are in Bethesda and will stay there. Both NIEHS and NCI have assured them that we will not force them to move to North Carolina.

New recruiting, and in some cases, replacing people who leave, is being done at Research Triangle Park.

NCI BIOASSAY PERSONNEL

Senator ANDREWS. Are you moving any of these people to North Carolina?

Dr. RALL. Three have moved voluntarily. We expect most of the others will not. It actually works out very well. The employees in Bethesda are involved in the contract monitoring, and business management part of the testing effort, and it is useful for them to be there near the contract administrators at NIH. The scientifically oriented aspects relating to test development and validation have tended to move to North Carolina.

Senator ANDREWS. So your effort is to move the scientific ones to North Carolina so they can all be together, and the contracting personnel who might as well be in a separate division will be up here.

Dr. RALL. That's right. And we can offer scientists, as our new laboratories are finished, some laboratory space to do their own experiments. We think that's terribly important.

Senator ANDREWS. Are you prepared from a staffing standpoint to handle such a major increase in budget?

Dr. RALL. Yes, we think so.

Senator ANDREWS. You say that with a smile?

Dr. RALL. I say that with a little less conviction than I would like to be able to. With the personnel freezes, it may be hard to get the additional contract specialists or toxicologists we need. But I cross my fingers and think we'll make it.

Senator ANDREWS. Well, I think it would be useful for you to let the subcommittee know what particular specialties you think you're going to need so we can be helpful to you.

Dr. RALL. We think it's going to be OK. The Department has a process of approving new hires within our personnel ceiling, and it's working. It's just that it tends to make us nervous. It's not like the old days when you could go out and hire someone quickly.

Senator ANDREWS. But don't these slots move with you?

Dr. RALL. Oh, yes.

Senator ANDREWS. Have you detected a long delay in transfer of the slots to you?

Dr. RALL. Oh, no. That's worked out very well.

Senator ANDREWS. So you have the slots you need. You are in the process now of finding the people to fill the slots.

Dr. RALL. That's right. Our contract program will increase from $10 to $50 million, and that is a very large increase. And I think if I weren't nervous and concerned about it, I wouldn't be a proper manager. That's a big increase.

Senator ANDREWS. That's the proper way to be, run scared. That's what we do each election year.

Does the transfer of the bioassay testing program from NCI to your Institute require legislation?

Dr. RALL. It does not require legislation. The Secretary could approve it. It was discussed with the committee last year, when the proposal was under consideration by the Secretary's staff.

Senator ANDREWS. An in-house directive by the Secretary is——

Dr. Rall. Adequate? Yes, sir.

Senator ANDREWS. Well, in this transfer of money from one account to another, do you do this simply by our appropriating it?

Dr. RALL. Yes, sir.

Senator ANDREWS. You can't move it within your area without reprograming and coming back and checking with the subcommittee, as I understand it.

Dr. RALL. Tony, I'm running out of expertise.

Mr. ITTEILAG. Senator, we cannot move money from one NIH appropriation to another without the approval of Congress. What we can do and what I believe we have done is when a function transfers from one appropriation to another, the rules of the game from a fiscal standpoint allow us to have the losing activity reimburse the gaining activity. In this case, the NCI will reimburse NIEHS in 1982. The 1983 requuest for NIEHS covers the program fully.

Senator ANDREWS. Has your General Counsel looked at that?

Mr. ITTEILAG. Yes, sir; that particular aspect of the situation I am comfortable with. What I am not comfortable with, I must say, is the fact we apparently have not advised the subcommittee on the matter in any formal way, and perhaps that is something——

Senator ANDREWS. You're precisely right. [Laughter.]

And if there is a General Counsel's opinion, we'd certainly like to see it and we'd appreciate it. Will you provide that for the record.

[The information follows:]

GENERAL COUNSEL'S OPINION

The transfer of the NCI bioassay program to NIEHS and an internal reorganization of NIEHS was accomplished under the Secretary's reorganization authority as specified in reorganization plan No. 30F 1966. It was approved by the Secretary July 14, 1981, and a notice was published in the Federal Register July 27, 1981.

The reorganization proposal was reviewed by the Office of the General Counsel prior to the Secretary's approval. In June 1981 the Office of the General Counsel cleared the request.

AGENT ORANGE

Senator ANDREWS. Doctor, one final question. There has been a lot of talk in the last year or two about agent orange—those of us who farm know it as 2,4,5-T—and a considerable concern over its impact on individuals. It looks like it's right down your alley. Have you been doing any work on agent orange?

Dr. RALL. In 1970, we were involved in the original investigation which showed that 2,4,5-T was teratogenic. We have been working on it constantly since then. I reported briefly last year a long study in which we looked at the effects of synthetic agent orange on——

Senator ANDREWS. You said 2,4,5-T was not teratogenic?

Dr. RALL. No, it was teratogenic.

Senator ANDREWS. Run that one by me again.

Dr. RALL. Our scientists in the early 1970's were the first to show that 2,4,5-T was teratogenic, caused birth defects.

Senator ANDREWS. 2,4,5-T as a pure chemical or as a dioxin.

Dr. RALL. As the standard contaminated chemical. But we then split it up. Dioxin is very teratogenic. 2,4,5-T as a pure chemical is somewhat teratogenic itself—not to the same extent as dioxin is, but it is teratogenic.

We have studied these series of compounds for the last 10 years. We reported on a study last year where these compounds had no effect on the male. The veterans, you remember, were complaining that although they were the ones exposed to agent orange, their wives had miscarriages and stillbirths.

We set up a study in rodents giving very large doses of a mixture of 2,4-D, 2,4,5-T dioxin to the male animals. We found no effects on fertility; we found no birth defects; we found no defects on sperm count or sperm shape.

It is only an animal study but at least it gives us some encouragement.

The Centers for Disease Control are trying to do an epidemiological study looking for birth defects among Vietnam veterans. NIEHS is setting up through the International Agency for Research on Cancer—part of the World Health Organization—a worldwide registry of people exposed to 2,4,5-T in various situations.

There are too few people in the United States who we know to have been seriously exposed to have confidence in the health data; but throughout the world, there have been a number of accidents where people have been exposed to 2,4,5-T. We are going to try to collect all that worldwide information and get a much better view of whether there is an effect in males.

There are repeated reports from the Scandinavian countries that applicators of 2,4,5-T, 2,4-D pesticides have soft tissue carcinomas in a rate that would exceed what you would expect. These are not the best conducted studies in the world; but they are very suggestive. There are two or three instances in the United States now that have been reported anecdotally that such workers have this same sort of soft tissue cancer. So we are following it very closely.

Senator ANDREWS. You said you have done the research on 2,4,5-T and found it's teratogenic but not to the extent that dioxin is. Have you also done similar research in-house on 2,4-D?

Dr. RALL. Yes, 2,4-D is not teratogenic. We are looking at it currently in a neurobehavioral study because people who have been exposed to 2,4-D have reported severe neurological problems which last a long time.

We are trying to reproduce this in rodents, and we simply don't know what the answer is yet.

Senator ANDREWS. But that work is ongoing?

Dr. RALL. It is ongoing.

Senator ANDREWS. I almost took a bath in that stuff over a period of 5 or 6 years. When you're spraying it as heavily as we are you can smell it a hundred yards away. You know how it smells.

SUBMITTED QUESTIONS

I have some additional questions, Doctor, but I would appreciate it if you'd provide the answers for the record at the same time as you return the corrected hearing transcript.

[The following questions were not asked at the hearing but were submitted for response for the record:]

Questions Submitted by the Subcommittee

IMPACT OF CONTINUING RESOLUTION

Question: What has been the impact of the 1982 Continuing Resolution which imposed the lower of the House or the Senate figures and a 4% reduction beyond that?

Answer: NIEHS has negotiated reductions in all ongoing research and center grants. These reductions will average 4 percent. Further, awards for the 104 competing grants which will be funded will be reduced, and approximately 4 percent of the competing grants provided in the Congressional allowance will not be awarded. Research training efforts will be reduced in order to meet the NIH policy regarding support of indirect costs, institutional allowances and stipend levels. Funds available for targeted research and toxicity testing will be reduced by 4 percent; and planned in-house research expansion in the fields of reproductive toxicology, genetic monitoring methods, and pulmonary toxicology will be deferred.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: In the NIEHS budget, direct operations and program management activities represent salaries and expenses. Increases in these activities are tied to mandatory personnel cost increases. However, NIEHS is looking carefully at such cost elements as travel and consultant services to determine if budget levels can be reduced to move funds into activities more directly related to our mission. NIEHS management is also carefully reviewing the cost of a number of supporting service activities more closely related to the research programs. Where the level of service or the benefit cannot be justified the financial support will be reduced or curtailed. Resultant savings will be directed to research programs.

Question: What are your most important administrative concerns -- and what are your least important concerns?

Answer: NIEHS' most important administrative concern is the occupancy of our new facilities. In addition to the significnt change this will make in our operations, the cost increment for utilities, operations and maintenance has been sizeable. Forecast increases to these costs take essentially all portion of our net increase from 1982 to 1983. Another administrative concern is the effect of research grant increases related to the NIH-wide stabilization initiative on our training and targeted research programs.

PROGRAM PLANNING

Question: How will the proposed budget affect your program planning for the coming year and where will you place your priorities?

Answer: The proposed budget increase from Fiscal 1982 to 1983 for NIEHS is 2.1 percent. Priority will be given to maintaining the Institute's share of competing research grant awards and maintaining the Fiscal 1982 levels of effort at our Environmental Health Science Centers. In addition, the Institute must meet the increased cost of operating facilities and supporting services for our Facility at Research Triangle Park.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: In order to achieve some degree of stabilization of investigator-initiated research, and to maintain the current level of in-house research effort, it has been necessary to reduce the budget levels for training support and for targeted research such as toxicity testing and test development.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982 and how much will you spend in fiscal 1983?

Answer: NIEHS is spending a total of $10,052,000 on Environmental Health Sciences and Marine and Freshwater Biomedical Centers in FY 82 and have budgeted $11,529,000 for FY 83. The FY 82 figure reflects a 6% reduction due to the Continuing Resolution.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: In FY 83 two types of economies could be implemented.

The estimated direct cost budgets for each center for FY 83 include an escalation over the FY 82 budgets. The estimated direct cost budgets can be negotiated downward.

New research projects and other activities scheduled to be initiated within the various centers in FY 83 could be delayed thereby decreasing costs in FY 83. These economies would postpone but would not prevent scheduled activities from being conducted.

REDUCTIONS IN FORCE

Question: Were personnel released from NIEHS in fiscal year 1982 due to budget restrictions?

Answer: We have not separated employees at NIEHS due to budget reductions or limited funds.

Question: Are any reductions in force planned for FY 1983?

Answer: At the level of the President's request, we will not need to separate employees due to budget restrictions.

GENERAL POLICY

Question: Please describe the current NIEHS attitude toward the environment, environmentally-related problems and the impact of such problems on the U.S. economy.

Answer: From my standpoint, the late 1940s and 50s, when many new drugs and other products made from synthetic chemicals first came on the market, was a period when we all placed a great faith in better living through chemistry. The 1960s and 1970s turned very gloomy with discoveries of environmental disasters involving Kepone, PBBs, and chemical dumps like the Love Canal. I hope that the 1980s will represent an era in which greater scientific understanding of the relationship between the environment and human health leads to a more realistic assessment, one which is likely to fall somewhere between these two extremes.

NIEHS conducts both basic and applied research into the effects of environmental elements on human health. We do not conduct economic analyses of either the cost of these diseases to our society nor do we estimate the costs to prevent these diseases.

A recent book published by the organization Resources for the Future, "Environmental Regulation and the U.S. Economy," states, "Considering their importance, there are surprisingly few comprehensive estimates of the costs of pollution control. Sometimes the information that is available is conflicting or disparate." I believe the same can be said for estimates of the burden of environmental damage. We know that the Adirondack lakes are now plagued by acid rain causing severe harm to both the environment and the fishing industry there, but I don't know that anyone has estimated the cost. Recently, Representative George Brown of California, a close observer of the effects of technology, estimated the cost of ozone damage in his home state alone at a billion dollars a year. As for health costs, we face the same paucity of good data. One estimate puts both direct and indirect (including health care and lost productivity) cost for cancer, which is to some extent preventable disease, as high as $25 billion.

In the environmental health sciences, we face similar problems to those of the mathematicians trying to weigh costs and benefits, the same problems of methodology and of data. Ours, too, is a very new field. The verdict is not in, and as a scientist, I'd have to say it may never be. But I don't think I can underestimate the need to conduct really good scientific research in order to answer questions about the effects of the environment on people's health.

Question: Please describe your Institute's attitude toward environmentalism today.

Answer: I would describe environmentalism as the belief that man is an integral part of the environment in which he lives and that significant harm to that environment can also constitute injury to man. At NIEHS we are dedicated to understanding these relationships.

Question: Given declining public sector budgets, especially in research and development, how will you attract and retain competent, dedicated researchers and scientists?

Answer: This has not been a problem for us so far. We are doing exciting work and our program has never had much difficulty attracting young, dedicated scientists and researchers.

Question: To what extent do you anticipate an increased workload from EPA and other similar agencies--and how will you handle it?

Answer: Because we are not a regulatory agency, I do not expect that our workload will increase.

ENVIRONMENTAL HEALTH ISSUES

Question: We understand that both the Environmental Protection Agency and the Energy Department will incur heavy cuts in their Environmental Health R & D programs, with some programs being terminated entirely. This means that the Environmental Health Sciences Institute may have to fill the void left by these cutbacks. How will proposed heavy cuts in EPA and DOE environmental health research budgets affect NIEHS programs?

Answer: NIEHS is sensitive to the possibility of reductions in the environmental health research budgets of these agencies. Some current collaborative activities with EPA and DOE may be affected. Should proposed budget cuts diminish basic research efforts at EPA and DOE, NIEHS in developing its plans will take into consideration needs in those areas of particular relevance to its own mission.

Question: Has there been a discussion of this issue with those agencies?

Answer: The Director, NIEHS and the Deputy Administrator, EPA have discussed the effect of EPA research and development budget cuts on basic environmental health research.

CUTBACKS IN ENVIRONMENTAL R & D

Question: What impacts will cutbacks in environmental health research and development in EPA and the Department of Energy have on your R & D programs?

Answer: As mentioned in an earlier answer, some current collaborative activities with EPA and DOE may be affected.

Question: To what extent will you be able to pick up on some aspects of EPA and DOE R & D programs under the present proposed budget?

Answer: Under the current budgetary situation it would be difficult to assume responsibility for relevant portions of EPA and DOE research and development programs. However, within current resource limits, NIEHS would take into consideration the needs created by cutbacks in research and development budgets. EPA's input into the National Toxicology Program would continue to be welcome.

Question: Have you been approached by EPA and DOE relative to proposed cutbacks in those agencies' Environmental health R & D and, if so, what was decided?

Answer: In discussions on topics of mutual interest, the Deputy Administrator of EPA did express concern to the Director of NIEHS over proposed cutbacks. No decisions were made.

Question: What is your position on these cutbacks and their impacts on environmental laws?

Answer: Responsibilities mandated under various environmental laws frequently require actions based on an adequate science base. To the extent that cutbacks hinder development of this base, effective implementation of the law will be affected.

Question: What steps would you recommend be taken to maintain and continue Federal Environmental Health R & D programs?

Answer: To maintain Federal environmental health research programs three things need to be done: the potential for serious health risk from exposure to certain environmental agents needs to be recognized; stable support for programs continued, with provision for some expanded funding in areas of particular promise; some relief from hiring restrictions granted, so that recruiting of the high quality of scientific staff can be sustained.

PROJECTS OF IMPORTANCE

Question: In the present atmosphere of increasing budget austerity, how much money will be allocated for specific projects you regard as of most immediate importance to the general public?

Answer: The programs at the National Insitute of Environmental Health Sciences involve a spectrum of activities ranging from basic research regarding metabolism and effects of chemicals on biologic systems, and the development of tests to assess toxicity, to the actual testing of specific chemicals. One of the major reasons for selection of a substance for toxicology testing is immediate importance to the health of the general public.

Also, results of other research performed at the Institute are available for application to numerous problems of immediate importance to the general public. Some of these problems are the potential health effects from hazardous chemical waste, chemical contamination of public water, asbestos in air, and contamination of the environment by PBBs and agent orange.

Question: What is the basis for calling these projects "of most immediate importance to the general public?" How do you rank these projects?

Answer: Importance to the general public is one of the major criteria applied in making choices about what research to pursue. A specific example is that the selection of chemicals for toxicity testing is based on recommendations from regulatory agencies, industry, and the public. Ranking of these projects is based on perception of widespread human exposure, potential for producing adverse health effects, and absence of adequate toxicologic information.

Question: Are any of these projects similar or identical to projects at the Environmental Protection Agency or the Cancer Institute? If so, please describe their differences and why your project requires continued funding.

Answer: The projects of the National Institute of Environmental Health Sciences are not identical or similar to those of the Environmental Protection Agency or the Cancer Institute. The projects of the EPA are determined by the regulatory mission of the EPA and the Cancer Institute has the understanding of a specific biologic end-point, cancer as its objective. The NIEHS is concerned with any potential health aspects of chemicals present in the environment.

Question: To what extent are such projects more individualistic or complementary--rather than reiterative?

Answer: The programs of the NIEHS are in many ways complementary to the programs of the EPA and the Cancer Institute. Knowledge of the potential toxicity of chemicals may assist the EPA in regulatory actions. The basic research and toxicity testing programs provide a broader range of health information than cancer per se, such as reproductive, neurobehavioral and genetic toxicology.

CHEMICAL WASTE

Question: The problem of stored chemical waste is not completely solved, and may cause future crises. Thus it is crucial to determine the adequacy of plans to handle future chemical waste crises. What work have you performed in relation to chemical waste, and what projects are planned for the future?

Answer: Concerns about the potential for chemical wastes to cause human health effects have come into sharper focus since the Love Canal, New York, problem in late 1978. Because of the questions arising from that problem, we organized a committee to review the state of the art for assessing human health effects from stored chemical waste for the DHHS. The report was issued in 1980.

Of the more than 300 chemicals identified at Love Canal, the National Toxicology Program had tested or was in the process of testing about 70 of them. The review stressed the importance of having methodology to test the neurologic, reproductive and genetic toxicology of chemicals. Also, this potential public health problem accentuated the need to increase capabilities to assess the toxicity mixtures of chemicals and to extrapolate risk to human health from toxicologic data. We have requested applications for research in these areas from scientists.

A multidisciplinary conference on the potential adverse health effects of toxic chemicals from waste dumps was held at NIEHS in October, 1981. Topics in which there is need for research were discussed. The proceedings of the conference will be published in an upcoming issue of the Environmental Health Perspectives.

Future plans include new research involving effects of mixtures of chemicals as well as continuing programs in reproduction and neurobehavioral toxicology, risk assessment, and testing of chemicals for toxicity. In addition, we have recently requested applications for research to identify early or pre-clinical indicators of effects of chemicals such as chromosomal abnormalities, abnormalities in sister chromatid exchange, and urinary excretion of altered products of DNA metabolism in populations that may have unique exposures.

Question: How much money and manpower are involved?

Answer: Most of the research programs of the National Institute of Environmental Health Sciences have some relevance to the stored chemical waste problem. Particularly significant are research programs in reproductive, genetic, and neurotoxicology, the findings of which may be directly applied to health problems resulting from exposure to toxic chemical wastes. However, no funds have been available for expansion or direct application of these programs to the specific problem of chemical waste.

Question: How will your project coordinate with EPA'S Superfund Program?

Answer: The Centers for Disease Control is the lead agency for coordinating the primary responsibilities for the evaluation of health effects due to chemical wastes and serves as the focus for coordinating with the Environmental Protection Agency's Superfund program.

Question: What provisions exist for interacting with the Federal Emergency Management Agency?

Answer: We have no provisions for directly interacting with the Federal Emergency Management Agency. Because the Centers for Disease Control has the responsibility for the Public Health Service for this coordination.

Question: Does the Institute have an organized emergency group ready to go out and help with chemical waste crises?

Answer: No, the emergency response responsibility is with the Centers for Disease Control. The NIEHS may provide toxicologic support when requested.

WATER QUALITY

Question: How do you enter into the water quality control picture in terms of the Federal Water Pollution Control Act, P.L. 92-500?

Answer: The Environmental Protection Agency (EPA) is responsible for implementing P.L. 92-500. As a biomedical research agency, NIEHS has no direct authority or responsibility under P.L. 92-500. However, NIEHS has studied the toxicity of agents which often pollute water and may effect peoples' health. Such agents include PCBs, asbestos fibers, trichloroethylene and other pesticide and herbicide residues. These agents may move into the food chain or contaminate drinking water.

Question: What work have you done in relation to surface and ground water quality?

Answer: NIEHS has done considerable research on the toxicity and the mechanisms of action of many synthetic agents found in both surface and ground water. Toxicity data from the National Toxicology Program tests are the major source of data on many chemical agents which have been found to contaminate some communities' water supplies.

Question: What work is planned?

Answer: As a part of the National Toxicology Program, NIEHS will continue to test agents of significant public health concern and unknown toxicity; further research to improve our ability to estimate varied risk at varied dose levels will continue. Inasmuch as many of these agents are involved with waste disposal problems, research funds authorized in the "superfund" may be used to support these studies.

Question: What coordination is planned between NIEHS and the various water quality control districts?

Answer: NIEHS does not have any responsibility to coordinate with these districts, however, NIEHS research findings are always available when assistance is requested. Further, NIEHS findings are passed promptly to the Environmental Protection Agency through a number of coordinating mechanisms.

TOXIC CHEMICALS

Question: What work has NIEHS done in researching the mechanisms of action of mutagenic, carcinogenic, and teratogenic chemicals?

Answer: NIEHS maintains an extensive program that seeks to identify chemicals that cause mutagenic, carcinogenic, or teratogenic effects. In FY '82, 458, 183, and 46 tests will be in progress in each of these 3 categories, respectively. The scope of these testing efforts continues to be expanded so that results may provide better insight as to the major factors associated with mutagenesis, carcinogenesis, or teratogenesis. In particular, how the structure of classes of chemical compounds and their metabolic products can be related to the cause of biological damage.

The utilization of biological tests in arriving at estimates of chemical hazards to health is considerably enhanced by knowledge of the basic mechanisms which are responsible for the initiation and expression of the health effect. The assurance that the mechanisms which cause the cellular damage can be generalized to several species, including higher mammalian organisms, reduces the uncertainty of extrapolating the results of biological testing to estimates of risk in human population.

NIEHS supports research that concerns the correlation of chemical structure of compounds and the initiation of carcinogenic, mutagenic, and teratogenic mechanisms. Emphasis has been given to PCB's, dioxins, polycyclic aromatic hydrocarbons, and several other classes of reactive organic compounds. The balance between metabolic pathways that increase biological potency, or activate the chemical, and those that detoxify or remove the chemical by conjugation determines the effective dose of the chemical exposure. Such knowledge is essential to the understanding of chemical structural determinants, dose-response relationships and estimates of risk.

These studies are prominent in the National Toxicology Program, the Intramural Research Program, and the Extramural Program.

MUTAGENESIS

The central questions of mutagenic mechanisms which are reasonably approachable in the near future are as follows. What are the enzymatic mechanisms of DNA fidelity as expressed through DNA polymerases and their associated proteins? What are the enzymologies of mismatch repair and error-prone repair? What are the paths from DNA damage to ultimate mutations? (This question has at least four components: the nature of spontaneous mutations, the mutagen specificities of diverse agents, the nature of responsive DNA sequences and the integrative aspects of mutational pathways involving error-prone and error-proof steps.) How is the body of knowledge developed in lower biological systems to be extended to humans?

An association has been demonstrated between mutational hot spots (the major determinant of a gene's mutational responses) and the potential of the surrounding sequence to form short, mis-matched loops of secondary structures. Originally noted in the E. coli lacI gene, this association has now been discovered in other E. coli and yeast genes, and may be very general. In a different kind of analysis, qualitative differences have been discovered in the kinds of point mutations produced by gamma irradiation as a function of dose, a result important to risk estimation. Finally, a system of mutation avoidance has been defined genetically by the discovery and characterization of mutants of E. coli that are defective in post-replication mis-match repair. This system may provide as much as 1000-fold protection against certain types of spontaneous and induced mutations.

The role of DNA polymerase in maintaining the fidelty of DNA replication has been studied by characterizing the propertise of mutant polymerase enzymes. It has been shown that bacteriophage T4 polymerases detect aspects other than hydrogen bonding strengths between base pairs to mediate accurate coding; for instance, antimutagenic polymerase reduces the frequency of certain classes of mispairs more than others.

Research has focused on mechanisms of DNA replication in both prokaryotic and eukaryotic systems. A prime effort has been to isolate DNA replication-defective mutants and to establish in vitro DNA replication systems. The first clear-cut mutations affecting the eukaryotic DNA replicase, polymerase alpha, have been isolated in a Drosophila cell line on the basis of aphidicolin resistance. One is a kinetic mutant and the other an overproducer. The same approach has been extended to yeasts, where it has been shown that DNA polymerase I is the DNA replicase and can mutate to aphidicolin resistance. A new in vitro yeast 2-μ plasmid DNA replication system has been developed whose origin and direction of replication are identical to those in vivo. This system will be very useful for purifying yeast DNA replication proteins, and in defining the mechanisms of mutation processes.

The major issues affecting the research program in the eukaryotic organism, Drosophila, involve the mechanisms by which gene activity is regulated during cell determination and differentiation. We do not yet understand how some genes are activated in specific tissues and repressed in others and how this determined state is inherited in somatic cells during growth and development. Genes consist of considerably more than the sequence encoding a polypeptide. We know for example that many genes are mosaic structures with sequences of unknown function interspersed with segments that encode the messenger RNA. We know that some DNA sequences are mobile and that their insertion into chromosomes can alter gene function. We do not understand the origin of mobile sequences, their role in spontaneous mutation, or their sensitivities to mutagens. We know that the position that a gene occupies in the genome can have a dramatic effect on its regulation, but we do not yet understand why. These unanswered questions assume great importance in considerations of the processes of mutagenesis and the impact of environmental mutagens on living systems.

A survey of restriction map variability of the chromosomal DNA around a specific gene in populations of Drosophila melanogaster and related species has been conducted. The primary purpose is to recognize and quantify the variation that occurs naturally. The results indicate that there is a great deal of insertion/deletion variation in the sequences flanking the transcriptional unit of alcohol dehydrogenase. Since all the lines surveyed showed "normal" alcohol dehydrogenase activity, these insertion/deletion differences may have little effect. Each variant was limited to one local population, that is, they do not seem to spread throughout the species as most polymorphisms do, suggesting that the insertion/deletions may have some deleterious effect. The significances of the insertion/deletion type of mutation in natural populations is only now becoming accessible to experimentation. It may be that a large proportion of spontaneous deleterious mutations are of this type. These initial observations lay the foundation for further survey, experimentation, and theoretical work on the causes and consequences of this type of genetic change.

The white locus of Drosophila melanogaster was cloned by capitalizing on the observation that a copy of a previously cloned mobile DNA sequence is inserted into the white locus in one of the mutant alleles. The DNA sequences flanking the insert in this stock were cloned and then tested for homology to the white locus using in situ hybridization to the polytene chromosomes. Subsequent molecular and genetic characterization of the locus has demonstrated that most mutations arising in laboratory stocks result from the insertion of a copy of one of several families of transposable DNA sequence elements. This observation changes dramatically our concepts of the nature and origin of spontaneous mutations in higher organisms and points clearly to new approaches to the investigation of the mutation process in mammals (humans).

Cloning of the white locus has allowed analysis of the basis for the dramatic elevation of spontaneous mutation rates in the progeny of crosses between members of particular strain classes of Drosophila. It has been shown that the burst of mutations, known as hybrid dysgenesis, results from the mobilization of a single specific transposable DNA element family (the P factor family in this case). The P factor transposon sequences have been cloned and they now, in turn, can be used to clone any specific locus in Drosophila where the sequence will integrate. The P factor activity can be mobilized at will by performing appropriate crosses and the desired insertion events can be recognized by screening for mutants at the locus that is desired in cloned form. This approach to the purification of specific eukaryotic genes is expected to revolutionize the study of the organization, expression and regulation of genes in the development of multicellular organisms.

TERATOGENESIS

Research has focused on the functional and structural dysgenesis of the mammalian genital tract induced by prenatal exposure to diethylstilbestrol (DES). These have included induction of long-term latent genital tract defects, such as sterility and vaginal, cervical or uterine cancers, as well as genital abnormalities which are obvious at birth. Examples of the latter are in the offspring of mice given DES during pregnancy; testicular abnormalities were seen in males while structurally altered fallopian tubes were seen in females. These defects were observed in DES exposed humans, one or two years after they were described in mice. Chemicals structurally related to DES have been used to distinguish the role of the estrogenic (hormonal) function of DES in the induction of genital dysgenesis. These same analogs have been used in a tissue culture system for the morphological and molecular differentiation of the fetal genital tract to study the cellular basis of the DES-induced defects. Studies of cell and tissue interactions during genital tract development in vitro have helped elucidate the cellular targets for DES. The synthesis and release of factors which mediate growth and differentiation of these tissues seem to be altered by DES. In addition to studies on the cellular target for DES action, experiments on the metabolism and bioactivation of DES by its target cells in vitro have started to demonstrate the important structural requirements for hormone activity or toxic activity. These studies have also included experiments on the intracellular mode of action of DES and its metabolites or analogs in exerting its hormonal effects. Current studies are attempting to correlate changes in the fetal reproductive tract induced by DES and analogs at the molecular and structural levels. Since many common environmental chemicals (e.g., DDT, PCBs, Kepone, some mycotoxins) are estrogenic (have DES-like activities), these studies on the mechanism of action of DES and structurally-related chemicals should provide a basis for extrapolation to other chemical species.

TCDD, the toxic contaminant found in agent orange, is a very potent, yet specific inducer of cleft palate when administered to the pregnant mouse. Studies are in progress using cell, organ and whole animal studies to determine the biochemical and molecular basis for TCDD teratogenesis. The results to date strongly indicate that TCDD causes cleft palate by a receptor-dependent process that interferes with the differentiation of the palatal epithelial cells.

Culture of whole rodent embryos at the peak sensitive period for teratogenesis is currently being developed to determine the mechanism of actions of various potential human teratogens including alcohol, anticonvulsants and thalidomide. It appears in most cases that teratogens or their metabolites have a direct affect on the embryo and disrupt specific sensitive tissues.

A line of mesenchymal cells has been established from the human embryonic palate and can be cultured under a variety of conditions. Certain cleft palate teratogens, such as cortisone, appear to disrupt the normal growth and differentiation of these mesenchymal cells. Research suggests that the teratogenic mechanism of these steroids involves a receptor-dependent process that alters the genetic machinery of the cell. These cells have also provided a cell line in which to screen for potentially harmful chemicals in the environment. A rapid, inexpensive method is needed to select for further animal testing the most likely potential agent from the thousands of chemicals which need to be tested. These human cells, developed at NIEHS, offer a number of unique advantages for a short-term test for possible human teratogens.

CARCINOGENESIS

There are several lines of evidence which support the idea that cancer development is a multi-stage process. In contrast most conventionally studied mutational changes can be described on the cellular level by a one-step transition. The presumed multi-stage progression of neoplastic development might be comprised of a number of mutational changes, or both mutational and non-mutational changes. To clarify the relationship between neoplastic transformation and somatic mutation (between carcinogenesis and mutagenesis) the transitions in neoplastic transformation need to be defined.

The objective is to understand the role of somatic mutation in the transition of normal diploid cells to malignancy. One approach is to determine whether the transition of a pre-neoplastic fibroblast cell line to the neoplastic stage is a mutational event, and to compare the ability of chemicals with high and low mutational activity for their transforming activity in the same cell system. The latter includes mutagenesis and transformation studies with diethylstilbestrol (DES) and other selected chemicals.

Results to date indicate that spontaneous transformation of syrian hamster fibroblasts occurs in at least two steps; that cells with the transformed phenotype arising at a rate consistent with a single locus somatic mutation; and that DES, a known carcinogen in humans and rodents is capable of causing neoplastic transformation of mammalian cells and under the same conditions does not induct somatic mutations at two genetic loci.

These studies provide strong evidence that cancer develops in stages. They also suggest that mutational events may indeed be an important aspect of the stepwise development of cancer. The studies with DES indicate that at least some chemical carcinogens can transform cells through mechanisms other than point mutation.

Future studies will examine the role of mutational events in other transformation systems and will attempt to establish the mechanism of DES carcinogenesis.

The most common fatal cancer in the United States is bronchogenic carcinoma. Clinical evidence suggests that bronchogenic carcinoma, like most other neoplastic diseases, develops over a period of many years and goes through several pre-neoplastic stages before the fatal invasive cancer emerges. It is therefore essential, besides developing cancer prevention methods, to develop means for identifying the early pre-neoplastic stages of bronchogenic carcinoma and to attain knowledge of the biology of pre-neoplasia. This is a prerequisite for designing effective intervention methods, which will arrest the progression from the pre-neoplastic to the neoplastic stage.

The objective is to obtain a basic understanding of the development stages of cancer in a rodent model of bronchogenic carcinoma and to develop biologic, immunologic and biochemical markers for early pre-neoplastic stages.

The changes developing in carcinogen exposed airway equithelium are analyzed with use of a cell culture assay.

The findings to date are that by this method cells can be identified and isolated immediately after exposure, which are characterized by a fundamental change in growth control (loss of growth is one fundamental characteristic of cancer), while normal airway epithelial cells senesce in vitro after few weeks in culture and die, cells from carcinogen exposed epithelium escape senescence and become "immortal". Some of the progeny of these cells become neoplastically transformed. It was further shown that during this progression from the pre-neoplastic to the neoplastic state, the cells acquire new antigens and frequently show dramatic shifts in DNA content. Both of these changes will become useful markers for identifying pre-neoplastic cell populations in culture.

It is possible to identify and select for the "carcinogen altered" cells long before cancer develops, and from these carcinogen altered cells the neoplastic cells develop through subsequent stages. Future studies will be concerned with characterization of cells in various pre-neoplastic states using biochemical and immunological markers.

Question: Have you issued public "notifications of risk" concerning exposure to chemicals which are mutagenic or carcinogenic?

Answer: NIEHS announces experimental and testing results in periodic open meetings, in scientific forums, in the NTP Annual Plans, in the NTP Technical Bulletins (to a mailing list of 5500), in the journal literature, and in NTP Toxicology and Carcinogenesis Bioassay Technical Reports (draft copies are distributed to other governmental agencies and to anyone on request; final peer-reviewed, printed versions are distributed as well as deposited at the United States National Technical Information Service). "Notifications of risk" are not per se formulated; the results with the evaluative scientific conclusions are issued.

Regulatory agencies are alerted during the data evaluation process for chemicals found to be carcinogenic in experimental animals. Federal Register notices and Department press releases contain brief summaries of results and announce availability of technical reports.

Question: How effective have you been in preventing exposure to these chemicals?

Answer: To estimate the real effectiveness in reducing exposure to chemicals known to cause toxicity in animals, and even for those fewer chemicals known to cause toxicity (and cancer) in humans, continues to be a particularly difficult (and near impossible) task. The question is perhaps better answered by the more intimately involved regulatory agencies; the NIEHS evaluates scientifically the experimental research and testing results and alerts these agencies as soon as is feasible. Further, the often long period between exposure to a chemical and the onset of disease (cancer for instance) makes equally difficult the association between actual cause and effect. Nonetheless, since chemically-induced toxic effects in animals predict for human response as well, reducing exposure to toxic or potentially toxic chemicals does reduce risk, even if quantitative estimates cannot be made with accuracy at this time.

Question: What progress has been made in developing techniques for preventing disease after exposure?

Answer: In addition to attempting to reduce or prevent exposure (the best technique for eliminating the chemically-induced disease), NIEHS has researched the effectiveness of accelerated removal of chemicals from the body of exposed victims. As examples, for one chemical, chlordecone (Kepone), with widespread population exposure the results have been promising and are used clinically. For two others, polybrominated biphenyls (PBBs) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, dioxin) the results have not been satisfactory. Studies of this type continue.

Question: What progress has been made in your Institute's neurotoxicity studies?

Answer: The overall goal is to utilize inter-disciplinary strategies in the behavioral and neuro-sciences to understand the cause of environmentally related human diseases affecting behavior and the nervous system. To achieve this goal, research is conducted in three broad areas: identification of laboratory procedures useful in assessing the role of environmental factors in the development of behavioral and neurological abnormalities, determination of mechanisms whereby environmental factors produce their behavioral and neurotoxic effects, and identification of conditions which predispose individuals to the behavioral and neurotoxic effects of environmental factors.

A battery of neurobehavioral tests has been developed and examined for usefulness in screening for neurobehavioral toxicity. Extensive study of eight chemicals (acrylamide, arsenic, chlordecone, lead acetate, triethyl lead chloride, methyl mercury, tetraethyl tin, and sodium salicylate) demonstrated that this battery is a sensitive indicator of motor dysfunction and changes in behavioral reactiveness to stimuli. In addition, methods were developed for summarizing the large quantities of data that are generated from experiments of this kind into a manageable form that provides a basis for comparing the neurotoxic profiles and the relative toxicities of many agents. Using this test battery, we have uncovered a previously undetected effect of low doses of 2,4-D which, in rats, persists after cessation of exposure.

A series of neurobehavioral tests for use with young (preweanling) animals has also been developed and is undergoing extensive testing. This battery includes tests of learning and memory as well as sensory, motor, and behavioral reactivity measurements. Sensitive and valid tests in this area are extremely important since the developing nervous system is particularly vulnerable to insult.

Receptor binding assays have been developed and characterized for use in detecting neuronal changes to environmental toxicants. It was found that modifications in the affinity and/or density of neurotransmitter receptors produced by toxicants can be a major step in delineating further studies concerning the mechanism of action of neurotoxicants. For example, these studies initiated a series of investigations which demonstrated that the dopaminergic system is most vulnerable to the central nervous system actions of acrylamide.

It is well known that the nervous system possesses excess capacity (functional reserve) which can be damaged and may go undetected by commonly used functional tests. Moreover, it can also adapt to damage (compensatory mechanisms). Both of these phenomena pose a problem in detecting subtle effects of toxicants on the nervous system. Thus, a major thrust has been to investigate ways in which compromises in the redundancy and plasticity of the nervous system can be assessed. This is important since it is reasonable to assume that if either a redundant system or a compensatory mechanism has been called into play the ability of the system to make further compensatory changes has been reduced. We have, therefore, explored the hypothesis that exposure to neurotoxicants produces a shift in the homeostatic balance of neuronal functioning which can be unmasked by challenging the organism to adapt to other stressors.

We have demonstrated that the dose-effect curves for psychopharmacological agents can be shifted by doses of environmental toxicants (e.g., acrylamide, triethyl lead) which do not produce any detectable overt effects. This has been useful in two ways. First, it has markedly increased the sensitivity of certain test procedures in detecting effects of toxicants. Second, by determining which psychopharmacological agent(s) is being affected, it provides clues for neurochemical studies into the mechanism (s) by which the toxicant is producing its effect. Using this approach, we have determined that both the serotonergic and muscarinic systems are intimately involved in the tremorogenic effect of chlordecone (Kepone).

By examining the ability of the organism to adapt to non-chemical stressors, we have also demonstrated that the hypothalamic-pituitary axis, which is highly sensitive to environmental challenge, is particularly sensitive to the effects of toxic agents (e.g., monosodium glutamate, magnesium, chlordecone) or at least plays a major role in amplifying their effects. As an example, we have shown that chlordecone (Kepone) is selectively taken up by the hypothalamus and pituitary. It affects both the hypothalamic-pituitary-adrenal and hypothalamic-pituitary-gonadal axes (reduction in hypothalamic β-endorphin, pituitary metenkephalin, serum prolactin, and corticosterone). In conjunction with these studies, we have demonstrated a sex-related difference in enkephalin levels in the pituitary which is regulated by estrogen. It appears that the effect of chlordecone on metenkephalin levels in the pituitary is due to its estrogenicity.

We have also demonstrated that rats exposed perinatally to microwaves or to noise, and which otherwise show no overt toxicity, are less able to cope in a swim stress test than control animals. It thus appears that continued investigation of the ability of the organism to adapt to stressors will provide an important approach to the study of neurotoxicants.

PHENOXY HERBICIDES

Question: What work have you done in relation to studying the human health effects of exposure to Agent Orange and Phenoxy Herbicides?

Answer: NIEHS has over the years provided much of the basic knowledge that established the toxic potential of these chemicals including teratogenic, carcinogenic, and systemic effects. More recently it conducted a series of animal toxicity tests which attempted to assess effects of a simulated Agent Orange mixture on male fertility and birth defects in offspring from these exposed males. The studies in mice did not detect any effects that were associated with Agent Orange exposure.

Through its grants program, it has funded studies on American workers involved in the manufacture of these herbicides. Further, it has initiated a study to establish an international dioxin registry whose objective is to determine if there is an excess cancer or other toxic risk in people exposed to this chemical contaminant of some phenoxy acid herbicides.

Question: What coordination has occurred between NIEHS and the Veterans Administration?

Answer: Coordination between the NIEHS and the Veterans Administration is effected through the Agent Orange Interagency workgroup. On behalf of DHHS, NIEHS chairs and provides administrative support of the chartered committee that oversees performance of the Air Force epidemiology study of its Ranch Hand personnel. (Ranch Hand personnel were the individuals who conducted the aerial application of Agent Orange in Vietnam.) The results of this study is of direct relevance and interest to the VA. The VA is invited to each meeting and is provided copies of the meeting transcript.

INDOOR AIR QUALITY

Question: What work has NIEHS done in relation to indoor air quality?

Answer: The National Institute of Environmental Health Sciences, through the grants program, supports a major study concerned with the effects of sulfur dioxide and respiratory particulates on health.

These pollutants are measured in various settings, including indoor environment, in six different cities. Findings are compared to parameters of human health, particularly pulmonary function.

The NIEHS also supports studies on the possible health effects of a number of pollutants found in the indoor environment including asbestos and formaldehyde, which are substances of major concern.

Question: What coordination has existed among your Institute and other federal agencies concerning standards for indoor air quality?

Answer: The NIEHS participated in the preparation of an interagency report on possible health effects of indoor air quality and in a workshop organized by the Environmental Protection Agency and the Department of Energy in December, 1980.

RISK ASSESSMENT

Question: What progress has the National Toxicology Program (NTP) made in developing reasonable methods of risk assessment?

Answer: Statistical methodology has been developed for modifying the experimental design of the NTP's two-year carcinogenesis bioassay. The proposed modifications should generate bioassay data that will permit more precise risk estimates at low-dose levels without adversely affecting the power of the bioassay for detecting carcinogenic potential. In addition NTP has supported the construction of a large computerized data base employing information abstracted from existing research publications of the results from animal cancer bioassays. This data base is being used to investigate a variety of issues relevant to the general problem of quantitative species extrapolation in carcinogenesis. A similar effort is being initiated to develop quantitative measures of mutagenic potency, to apply these measures to a large data-set of Salmonella test results from the NCI/NTP, and to assess the extent to which these measures are dependent on various assay parameters such as the source of the metabolic activation mixture. Ultimately, an attempt will be made to quantify the degree of correlation between these indices of mutagenic potency and corresponding measures of carcinogenic potency generated in the related carcinogenesis research project. Finally, NTP scientists are conducting an active research program in the development of appropriate statistical procedures for the analysis of data arising from short-term mutagenicity tests. (Such analyses can provide a qualitative indication of mutagenic risk.)

Question: How will the NTP interact with EPA in developing and using risk assessment methodologies?

Answer: At the present time a joint EPA-NIEHS research project is being initiated that will attempt to develop more sophisticated approaches to the problem of quantitatively modeling teratogenic responses and extrapolating such effects across species. Besides addressing an important scientific problem in its own right, this research effort could serve as the basis for a more formal interaction between NTP and EPA in the future with regard to other risk assessment issues.

Question: What provisions exist for input from experts outside the NTP and EPA to help ensure development of valid risk assessment methodologies?

Answer: The NTP Board of Scientific Counselors, which is composed of eight distinguished scientists who are employed outside the federal government, provides scientific oversight of the NTP and thus has direct input into all NTP risk assessment research. For example, at the upcoming March Board Meeting NTP scientists, Board members, and an ad hoc group of international experts will address the issue of the design of the two-year cancer bioassay and its possible modification to increase its potential use in low-dose risk estimation.

NIEHS RESEARCH FACILITY

Question: Dr. Rall, I'm sure you know of our Subcommittee's interest in your problem with the contractor and subcontractor's on your new facility in North Carolina. We gave you $2.4 million in reprogrammed funds to prepare your defense against claims by the subcontractors. Please bring us up-to-date on this matter. When will it be resolved? What has been done with the money we provided? We assume it will be enough.

Answer: Of the $2.4 million authorized by the 1981 reprogramming, $750,000 was made available for a contract with Kellogg Corp. to provide an independent analysis of the extent of government liability in this matter and to prepare materials for use in defending against subcontractor claims. The total cost of the Kellogg contract is $1,049,000; the Department had authorized $310,000 for this effort prior to the reprogramming request. The remaining $1,675,000 of the reprogrammed funds is being used to fund authorized changes in the construction project, correct deficiencies in design, intensify final inspection procedures, and reimburse the Construction Manager for work through the remainder of the project.

Although the funds provided are adequate to finish the project, a number of subcontractors on this project have filed claims due to delays in scheduling and alleged design defects. Current subcontractor claims total approximately $13,000,000. We anticipate additional claims amounting to $5 million to $7 million. It is estimated that it will be late 1983 or early 1984 before the final extent of government liability in these claims is determined. The majority of large claims have been appealed to the Armed Services Board of Contract Appeals (ASBCA). Decisions of the ASBCA are appealable to the Court of Claims. This is the normal time frame required for such appeals. It is impossible at this point to say what additional funds will be needed to settle these claims, because settlement depends first of all on the findings of liability by the ASBCA or the Court of Claims and then their decisions as to the amount of compensation. If funds are needed beyond what is presently available to cover the government liability they will be requested through the appropriation process.

The final Kellogg report is expected to be available within several months. Since the Government has taken the position that findings are privileged from a litigation standpoint, it is not appropriate to discuss the Kellogg's preliminary findings for the record. The Department believes, however, that these findings will be beneficial to the Government in pending litigation.

SUBCOMMITTEE RECESS

Senator ANDREWS. The subcommittee will stand in recess until 2 o'clock this afternoon. We will meet again in this room.

Thank you very much.

[Whereupon, at 12 noon, Tuesday, February 23, the subcommittee was recessed, to reconvene at 2 p.m. the same day.]

(AFTERNOON SESSION, 2:12 P.M., TUESDAY, FEBRUARY 23, 1982)

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF DR. THOMAS E. MALONE, ACTING DIRECTOR

ACCOMPANIED BY:

- DR. WILLIAM RAUB, ASSOCIATE DIRECTOR FOR RESEARCH AND TRAINING
- DR. JOSEPH E. RALL, ACTING DEPUTY DIRECTOR FOR SCIENCE
- CALVIN B. BALDWIN, ASSOCIATE DIRECTOR FOR ADMINISTRATION
- NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT
- ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator SCHMITT [presiding]. The hearing will come to order. I apologize to everyone for the late beginning, but I'm afraid it's going to be one of those afternoons. We are back on the Department of Justice authorization bill. There is a cloture motion that has been invoked, and I suspect there will be a few rollcalls. We'll do the best we can, trying to finish today. If we can't, we'll either handle it for the record or a later date.

This afternoon we will continue with the subcommittee's fiscal 1983 hearings on the National Institutes of Health.

Our first witness this afternoon will be Dr. Thomas Malone, the Acting Director of NIH, who will provide us with an overview of the NIH budget.

Dr. Malone, let me personally compliment you on your guidance of the Institutes during this transition period. You certainly have provided the appropriate stewardship for that time, and I want you to know the subcommittee appreciates it, and it probably has been difficult, having had my own experience in an administration, and we certainly appreciate it.

If you would introduce your colleagues and briefly summarize your opening statement—the total text will be included in the record—then we'll go to questions.

INTRODUCTION OF ASSOCIATES

Dr. MALONE. Thank you, Mr. Chairman, for those kind words. I am accompanied by Dr. William Raub on my left, the Associate Director for Research and Training at NIH, and on my right by Mr. Norman Mansfield, Director, Division of Financial Management. Behind me is

Dr. Joseph Rall, Acting Deputy Director for Science, and to the far right is Mr. Anthony Itteilag, Deputy Assistant Secretary for Budget.

NIH PROGRESS AND ACHIEVEMENTS

I welcome this opportunity to testify on behalf of the President's 1983 budget request for the National Institutes of Health. It is almost anticlimactic.

I would like to repeat something I said yesterday, and that is that the programs of NIH have moved forward steadily during the past year. This is because of the tradition of excellence and achievement built upon the high quality and depth of resources, both in terms of people and technology made possible by the continuing support of Congress and certainly through the efforts of Secretary Schweiker.

I would like to say simply that the commitment of public support for NIH has been a notable success. We think we have a research capability second to none. And we now have moved over the last three decades into a biological revolution described by many of the Institute Directors.

Many of them described the phenomenal progress we have made in genetics, the remarkable and spectacular tool that we now have in recombinant DNA technology, allowing us to transfer hereditary units from one species to another, thereby affecting evolution in the laboratory, and permitting, for example, bacteria to become factories producing pure hormones and substances of biological, agricultural, and medical importance.

We can, indeed, program a malignant cell to produce large quantities of antibody against a specific antigen. This so-called hybridoma technique has the possibility before the year 2000 for elaborating the millions of antibodies of the human body that we can use in combating disease.

We have heard also today about the exciting discoveries in cell transformation in vitro. We know a bit more about how the DNA molecule controls protein synthesis, both in normal and in cancer cells. We have heard that we have come a great distance in understanding that most marvelous organ, the brain, and with the use of revolutionary technology we can study the metabolism of the brain in a noninvasive way.

We have not just accrued knowledge. We have translated much of this knowledge into useful interventions that have improved the health status of millions of Americans and people all over the world. We will have some examples of these interventions, I am sure, when we hear from the remaining speakers this afternoon.

Secretary Schweiker has established a departmental objective placing the highest priority on actions to prevent disease, and we have joined with him in that activity.

BUDGET REQUEST

I believe that the administration's 1983 budget for the National Institutes of Health reflects a continuing commitment to its progress and to biomedical research. The Secretary of HHS and the President have been supportive of our programs, and they have presented a budget that will allow us to continue the challenge of this biological revolution.

The budget shows an increase of $108.5 million over the 1982 level. It allows us to continue to place high priority on the support of investigator-initiated research projects, from which the most promising scientific discoveries will come. We will support a total of over 15,000 such grants.

We hope to maintain program balance, because research project support is a substratum from which there must emerge applications of research and technology transfer. We believe that, with the funds allotted for research training, we can realize the reciprocal relationship that must occur between the continued productivity of research and the production of new investigators.

The 1983 budget does assume a 10-percent reduction in reimbursement for the indirect costs associated with research grants. We recognize that this is an important item, that indirect costs are real costs in doing research, but we also recognize that we and the grantee institutions cannot continue to allow these costs to become an ever-larger fraction of the total. The 10-percent reduction in reimbursement provides a way for us to contain this expenditure immediately while we set the stage for cooperative efforts with grantee institutions to find better ways to control indirect costs at the local level. We expect that the NIH Director's advisory committee will be useful to us in these determinations.

Finally, we do have our share of issues to pursue within the context of this budget. We must continue to search for greater efficiency in the use of research funds. We intend to work and are working with other research agencies to revitalize those aspects of research that might have deteriorated over the last decade. We are attending to the issues of accountability, both scientifically and fiscally, and we are trying to find ways to strengthen government-university-industry cooperation in research, recognizing that there can be no substitute for the Federal Government as a major source of support for basic research.

Mr. Chairman, I would be pleased to answer any questions you may have after this brief summary of my overview.

PREPARED STATEMENT

Senator SCHMITT. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. THOMAS E. MALONE

I welcome this opportunity to testify on behalf of the President's 1983 budget request for the National Institutes of Health (NIH).

As you know, I have served as Acting Director of NIH since the departure last July of Donald S. Fredrickson.

The programs of the NIH have moved forward steadily during the past year. This is because of the tradition of excellence and achievement built upon the high quality and depth of resources--in people and technology--made possible by the support of Congress and certainly through the efforts of Secretary Schweiker.

Indeed, the commitment of public support for biomedical research has been a phenomenal success and, as observed recently by a former member of the President's Cancer Panel, is "one of this nation's original contributions to civilization during the three and one-half decades since World War II." We have research capability second to none, a capacity enhanced through our cooperation with scientists throughout the world. The results of this research have made a healthier world, and an ever-expanding knowledge base promises to unlock the mysteries of those diseases that still plague humanity.

I would be remiss if I did not remind this committee of some of the achievements in biomedical research that have brought us to the threshold of a "biological revolution," a revolution that is allowing us to decipher the inner secrets of life at a rate that we would not have imagined even a few years ago. You will hear more detailed testimony from our Institutes on such advances, but I want to set the stage for their remarks by citing one or two examples of this epochal expansion.

Over the last two decades we have discovered the genetic basis for over a thousand disorders. One of the earliest was the finding that a change in one amino acid in a chain of 280 in the hemoglobin molecule produced the condition of sickle cell anemia and all the misery that goes with it.

Following the discovery earlier in this century that DNA was the material basis of heredity, scientists rapidly discovered how information was encoded in DNA, how such information was transcribed and translated to form cell substances, and how this material was copied to be shared with future generations. We are proud that Dr. Marshall Nirenberg of the NIH solved the genetic code in the early sixties. This was one of the most important discoveries in biology in the century and Nirenberg appropriately received the Nobel Prize for it.

The development of recombinant DNA technology gave us perhaps the most spectacular and exciting tool of recent times, allowing us to transfer hereditary units from one species to another and permitting, for example, bacteria to become factories producing pure hormones and substances of biological, agricultural, and medical importance. Recombinant DNA technology also can produce large quantities of pure antigen that can in turn be used as vaccines for immunization against infectious agents.

In addition, we can program a malignant cell to produce large quantities of antibody against a specific antigen. This so-called hybridoma technique gives us the possibility for elaborating eventually the 10 million or so potential human antibodies as an armamentarium against disease.

Quite recent and exciting discoveries have been made about what causes transformation of cells in vitro. Transformation is generally considered to be equivalent to the development of cancer in animals. Now it has been shown that some viruses transform cells because they produce a special protein causing cell multiplication--but this protein is very similar to a protein produced by the normal cells themselves. Even more remarkable is the finding that a few viruses transform cells just by causing the cells to increase the production of a protein the cells normally synthesize anyway. We now begin to have a clearer notion of what happens to the vast complexity of a cell's machinery when it becomes cancerous.

We have come a great distance in our quest to understand the human nervous system and new technologies give us unheralded possibilities. A revolutionary technology--the PETT Scanner (Positron Emission Transaxial Tomography)--provides a noninvasive way to study brain function and metabolism in living subjects. It is highly regarded as one of the most promising and versatile of research instruments. Scientists using PETT have identified the first metabolic differences that appear in the brains of schizophrenics. The instrument is also used in making decisions about when to operate on brain tumors and to pinpoint the trigger site of seizure in epilepsy. Within our intramural program, an advanced version of the PETT Scanner--the Neuro-PET--has been fabricated and is just becoming operational.

But we have not just accrued knowledge; much of the research has been translated into useful interventions that have improved the health status of millions of Americans, often with great economic returns. Just two examples will suffice to make the point now.

During the past decade, the death rate (age-corrected) for heart disease fell 25 percent, and the death rate from stroke fell 37 percent. Translated to number of lives saved, this means that at least a million more Americans are living today because of progress in cardiovascular research.

Ten years after the landmark legislation that intensified the nation's effort to conquer cancer, our most recent data show that 45 percent of all patients diagnosed with cancer from 1973 to 1979 are curable. Secretary Schweiker has transmitted to Members of Congress the publication of the National Cancer Advisory Board outlining progress made over the last decade and the clear promises for the future. Among an array of exciting new initiatives, the NCI has started a new program focusing on preventing various forms of cancers with chemo-preventive agents--substances that have been shown in animals to interfere actively with the cancer causing process.

Health promotion and the prevention of disease are the ultimate goals of our research and it is the highest form of cost-containment in the battle to reduce the rising cost of health care.

Knowledge acquired through basic research provides the foundation for prevention activities. The development of the polio vaccine is an example of the impact of preventive measures which had their roots in biomedical research.

Secretary Schweiker established objectives for Departmental emphasis and has placed highest priority on actions to prevent disease. As part of this initiative, in October 1981 we created at NIH a Special Assistant for Research Related to Disease Prevention. Dr. John Seal, who was assigned to this task, has the responsibility for coordinating an overall NIH Prevention Program, with the objective of stimulating added attention to prevention-related research and better inter-relating NIH activities with some of the specific objectives of the overall Departmental program. I believe we can now look to added benefits to the American people through more effective use of knowledge at hand to prevent the onset and progression of many diseases.

The Administration's 1983 budget for the National Institutes of Health reflects this commitment to biomedical research. The Secretary of HHS and the President are supportive of the NIH programs and have presented a budget that will allow us to continue to meet the challenge of the biological revolution. The FY 1983 budget for NIH is $3,748,771,000. This represents an increase of $108,585,000 over the 1982 level of $3,640,186,000.

The FY 1983 budget continues to place priority on the support of investigator-initiated research project grants, from which the most promising scientific discoveries will come.

In keeping with this priority the NIH will fund an estimated 4,100 new and competing research project grants and continue to spend 50% of its budget for research project grants, supporting a total of over 15,000 such grants. Other mechanisms of support provide the bridge between basic research and improved health promotion, prevention, and care. Program balance is thus a key consideration in determining the support levels for investigator-initiated research, and reflects the unique federal role in the area of biomedical research.

In striving to achieve program balance, the close and reciprocal relationship between the continued productivity of research and the availability and renewal of the supply of investigators is highlighted. Approximately 8,915 research trainees will be supported in 1983.

The FY 1983 budget request assumes a 10% reduction in reimbursement for the indirect costs associated with research grants. Although we recognize fully that indirect costs are real costs and are important expenditures affecting the strength and quality of the biomedical research environment, we also recognize that we and the grantee institutions cannot continue to allow these costs to become an ever-larger fraction of the total. The proposed 10% reduction in reimbursement provides a means for NIH to contain its expenditures in this area immediately and sets the stage for cooperative efforts with grantee institutions to find better ways to control indirect costs at the local level and to determine the nature and extent of the reimbursement that should come from public funds. We expect the NIH Director's Advisory Committee to be an invaluable forum for these efforts.

I am pleased to report that the new Ambulatory Care Research Facility was dedicated on October 22, 1981, thus adding a new capability at NIH for multidisciplinary, ambulatory research. The construction schedule has been essentially adhered to.

The budget includes $6.6 million for the fifth year of the modernization of our 500 bed hospital. These funds will be used to renovate patient care units and to correct obsolescence in nursing station units, medical support systems, and utilities. In addition, $5.0 million is included to start the rehabilitation of laboratory buildings to correct serious safety hazards and to upgrade labs to modern standards. These changes will allow us to maintain a center of unrivaled excellence whose scientists have shared in over one-third of the last eleven Nobel Prizes in Physiology or Medicine and who have produced over the last 20 years many of the most frequently cited research publications.

I would be less than candid if I did not say here that we have our share of issues to pursue if we are to maintain world leadership in biomedical research. In addition to the strategies mentioned earlier, we must continue to search for greater efficiency in the use of research funds. We must work with other research agencies to find ways to revitalize the country's instrumentation base and other resources needed for biomedical research. We must attend to the issues of accountability in both scientific and fiscal matters. We must improve, where necessary, our policies pertaining to the use of both animals and humans in experimentation and we must find ways to strengthen government-university-industry cooperation in research, recognizing that there can be no substitute for the federal government as a major source of support for basic research.

Mr. Chairman, I thank you and the Members of this Committee for the opportunity to present these general views on the FY 1983 budget for the National Institutes of Health. They will be complemented by more specific information in the testimonies of the Directors of the Institutes. We hope that this information will be valuable to you in the decisions you must make in the allocation of public resources. I will be pleased to answer any questions you may have.

BIOGRAPHICAL SKETCH

MALONE, DR. THOMAS E.
Acting Director, National Institutes of Health

June 3, 1926, Henderson, North Carolina.
Married, two children.

Education: Morehouse College, 1943-1945. B.S., North Carolina College, 1948. M.S., North Carolina College, 1949. Ph.D., Harvard University, 1952.

Professional History: 1950-1952, Teaching Fellow, Harvard University, Cambridge, Mass. 1952-1958, Assistant Professor of Zoology, North Carolina College, Durham, N.C. 1957, 1958 (summers), Lecturer in National Science Foundation Institutes for High School Teachers of Science and Mathematics. 1958-1960, Resident Research Associate, Argonne National Laboratory (Postdoctoral Fellowship recommended by National Academy of Sciences-National Research Council). 1960, National Science Foundation Panelist for reviewing proposals submitted for projects in science education and research. 1960, Assistant Professor of Biology, Loyola University, Chicago, Ill. 1961-1962, Visiting Lecturer, Evening Division, Illinois Institute of Technology, Chicago. 1962 (summer), Director, Summer Science Training Program for High-ability Secondary School Students of Loyola University, Chicago. (sponsored by the National Science Foundation). 1962, Grants Associate, Division of Research Grants, National Institutes of Health. 1963-1964, Assistant Chief, Research Grants Section, National Institute of Dental Research, NIH. 1964-1966, Deputy Chief, Extramural Programs, NIDR. 1966-1967, Chief, Periodontal Diseases and Soft Tissue Studies, NIDR. 1967-1969, Chairman, Department of Biology, American University of Beirut in Lebanon. 1969-1972, Associate Director for Extramural Programs, NIDR. 1972 to March 1977, Associate Director for Extramural Research and Training, NIH. March 1977 to present, Deputy Director, NIH. July 1981 to present, Acting Director, NIH.

Professional Organizations: American Association for the Advancement of Science, American Association for Laboratory Animal Science, American Society of Zoologists, The Histochemical Society, American Society for Cell Biology, International Association of Dental Research, Sigma Xi.

Honors, Awards: Harvard Fellow, 1950-1952. NAS-National Research Council Fellow, 1958-1959. DHEW Superior Service Award, 1970. DHEW Distinguished Service Award, 1974. Certificate of Merit, The American College of Dentists, 1975. U.S. Government Senior Executive Service Presidential Merit Award, 1980.

BIOLOGICAL REVOLUTION

Senator SCHMITT. Thank you, Doctor. I understand what you mean by "biological revolution." I have used the term myself, although sometimes I have said "a biotechnology revolution," but even that is probably not entirely accurate.

It seems to me that what we are seeing and have been experiencing and in some cases a party to is a revolution in the understanding of natural biomechanisms, ranging from the genetic code to the chemicals to the electrical systems that govern not only the body's normal activity but its response to disease and injury, including injury that we inflict on ourselves.

Would you agree with that general assessment of what's happening? It is not as easily said as "a biological revolution," but it may be more precise.

Dr. MALONE. You have put it more eloquently than I could have, sir.

Senator SCHMITT. It is extremely exciting because it means that we are headed toward a time when we not only can better anticipate disease, but should the body's natural mechanisms prove inadequate, or its organs cease to function or function inadequately, we are learning far more than we ever knew before about how to cure disease, and in fact cure injury by substitution of parts, as the case may demand.

In fact, as I have said many times before and will continue to say, I see this as the only alternative, the only acceptable alternative, to controlling somewhere in the future the ever-rising cost of health care, basically to avoid treatment—avoid it by preventing disease and injury, where possible, and avoid it by curing the disease or injury if it in fact occurs.

So the National Institutes of Health in a sense is our frontline of defense in building the basis of understanding and the application of that understanding to these very noble efforts.

If we are not successful, if you are not successful, and if the application of the research that you create is not successful to the extent that we do, in fact, gain control of health-care costs, then literally the country will go bankrupt. Because I don't see us in any near term putting a maximum value on human life, that if a cure of disease or injury exceeds that value we say, "Tough luck; you are not entitled to that cure."

What the people of this country and in the long term the people of the world are entitled to is protection from disease and injury, since we now have in hand and are developing further an understanding of how to do that. And it is an obligation you have and we have and everyone has, to the American people and to the people of the world, to provide the application of that understanding to their well-being.

Now, one area of understanding that we clearly have, and clearly have been unable to do anything about, is the rising impact that bad habits have on our health, not only throughout our lives but increasingly among the elderly as that population grows.

SURGEON GENERAL'S REPORT ON SMOKING

We frequently cite the case of cigarette smoking, and I notice in today's Washington Post we have another major report made public, issued by the Surgeon General, on the hazards of smoking. This report seems to go farther than any previous report. Of course, I have only seen the newspaper version of it. I expect we will get a copy soon.

But according to the Washington Post, smoking may cause nearly one-third of all cancer deaths. Cigarette smoking is clearly identified as "the chief preventable cause of death in our society," and though evidence is far from conclusive, nonsmokers who breathe the air where there is cigarette smoking also run the risk of cancer.

I would ask you, Dr. Malone, for your comments on this study. I know Dr. DeVita of the Cancer Institute is with us today, and we will talk with him in detail later, but maybe between the two of you you can give us at least an initial impression of this report and its consequences, possibly to a more broad recognition of the dangers of these bad habits that we have that are a leading ultimate cause of death and disease today.

Dr. MALONE. Yes, I would be glad to make some general comments and then leave the more specific technical aspects to Dr. DeVita. I believe that the first report of the Surgeon General was impressive enough, and now with the intervening years, with the accumulation of additional epidemiological data, it is quite clear that the prevention of disease, cancer in this case, can be directly ascribed to one's own lifestyle.

It is extremely difficult to get one to change a behavior pattern. There has been some success with teenagers, but an increasing number of women smoke, for example. All the evidence points to the fact that if one does stop smoking, one can add years to one's life, not only with regard to prevention of lung cancer but also of adjunct conditions.

It seems to me that we do have to place increasing attention on the business of promoting healthy approaches to living. I would hope that this report would be the substratum, the basis for doing that.

Senator SCHMITT. Were you surprised at the results of the study?

Dr. MALONE. No, I am a convert; and we are the worst of the lot.

Senator SCHMITT. Want to bet? [Laughter.]

Dr. MALONE. I was converted after the first Surgeon General's report. But I have great faith in the data as presented in this most recent report.

Senator SCHMITT. Do you expect to see the Institute change its course of research and training strategies as a consequence of this report and other new evidence on the bad habits problem?

Dr. MALONE. I believe that the Cancer Institute has contributed to the study. Smoking is an important program within the Cancer Institute; it is maintaining about the same level of support in 1983 as it did in 1982, devoting about $10 million to that effort. In addition, the National Heart, Lung, and Blood Institute is working on the problem, the Child Health Institute to a lesser extent, and also the National Institute of Environmental Health Sciences.

Senator SCHMITT. Do you have a coordinating team that ties these various efforts together?

Dr. MALONE. Yes; the coordination that occurs is essentially informal between these Institutes. However, there is a focus for smoking coordination in the Public Health Service, in the Office of the Assistant Secretary for Health, and the NIH participates in that general effort.

Senator SCHMITT. Do you find that adequate to prevent duplication so the broadest use of resources is possible—unnecessary duplication?

Dr. MALONE. I think the Public Health Service focus does prevent unnecessary duplication; yes.

EFFECTS OF MARIHUANA SMOKING

Senator SCHMITT. Is it your impression—and maybe I should ask Dr. DeVita to comment now, whatever other comments he may want to add to yours—but is it also your impression that smoking in general, including that of marihuana, would have similar implications beyond the other effects of marihuana smoking?

Dr. MALONE. I would defer to Dr. DeVita.

Dr. DEVITA. The volume of smoking of marihuana by an individual is somewhat less than that of a one- or two-pack-a-day smoker.

Senator SCHMITT. So you think from the basic smoke qualities, it is a question of quantity rather than just what type of smoke?

Dr. DEVITA. It is unlikely that burning marihuana will result in materials that are not carcinogenic, although we know less about the actual materials in the gas and particle phase in marihuana smoke than cigarette smoke. But clearly if the volume of exposure were equivalent, I would estimate that the damage to the lung, cancer or emphysema or both, would be equivalent.

Senator SCHMITT. Do we have enough experience yet with marihuana—I am not advocating more—but do we have enough experience with marihuana to see any evidence that this has been the case?

Dr. DEVITA. I don't know of any, Mr. Chairman.

Senator SCHMITT. Has there been a definitive analysis, an analytical comparison of the chemical products in marihuana smoke versus that in cigarette smoke?

Dr. DEVITA. I've never seen any as detailed as we have in cigarette smoke.

Senator SCHMITT. Don't we have the analytical capability to do that? Wouldn't that be something you could run down to the office and bring back here by 5 o'clock? [Laughter.]

Dr. DEVITA. I don't know.

Senator SCHMITT. Are you really telling me that nobody has ever made a study——

Dr. DEVITA. I'm not sure. I personally don't know. I'd have to check that.

Senator SCHMITT [continuing]. Of the chemical comparison of those types of smoke?

Could somebody research that for us and give us whatever summary information might be available?

Dr. MALONE. Yes; we will be pleased to do so.

Senator SCHMITT. Do you have any other comments, Dr. DeVita?

Dr. DEVITA. No, I agree with Dr. Malone the report represents very accurate data. There are some interesting positive sides of the report. Although the same number of people are smoking today that were smoking, say, a decade ago, the fraction of people smoking is less, and now for the first time we've seen a turnaround in the incidence of smoking, the prevalence of smoking amongst teenagers, both male and female.

In terms of disease prevention, there is quite clear evidence, as pointed out in the report, that if you don't smoke at all or you smoke for only short periods of time, it's easier for a person to stop. So if we can prevent our teenagers from starting, that will be very helpful.

Senator SCHMITT. Where does that information come from?

Dr. DeVita. There are epidemiological studies looking at the prevalence of smoking amongst the teenage population.

Dr. Malone. Dr. DeVita, I think the National Institute of Drug Abuse also probably has a good deal of data on teenage smoking.

Dr. DeVita. Yes.

Dr. Malone. We might try to seek from them some of the results.

Senator Schmitt. It seems to me at the very least someone would run an analysis to see if any of the apparent carcinogens in cigarette smoke are also present in marihuana smoke. I can't believe that hasn't been done.

Dr. DeVita. It may well have been done. When I sit down I'll ask a few people in the audience, Mr. Chairman. [Laughter.]

Dr. Malone. I believe the National Academy of Sciences was commissioned to do a study on marihuana, and I believe that study is about to be released. In any event, we will search it out and will see that you get the report.

RISKS OF ALCOHOL CONSUMPTION

Senator Schmitt. Dr. Malone, do you think that our understanding and perceptions of risk relative to alcohol, which are quite different in nature but the effect is unfortunately quite similar in terms of health-care costs to cigarette smoking—do you think those perceptions are as great as they are now for cigarettes?

Dr. Malone. This is a subject that is quite far afield for me, but I can venture to say that the NIH has nowhere near the data for alcohol consumption as the kinds of studies that have been done with respect to cigarette smoking. I would surmise that we are some distance from producing reports on alcohol in the same way that we contribute to the smoking reports from the Surgeon General.

Senator Schmitt. Well, the alcohol reports tend to come in more dramatic ways, such as the most recent study of accidents related to alcohol which shows in my home State 65 percent of the highway fatalities are alcohol-related.

Dr. Malone. Yes; I would certainly think that alcohol consumption is a problem of similar magnitude, and it has devastating side effects when innocent victims are killed by those who have been drinking. The statistics are quite impressive. I must agree that the problem is also a national dilemma, and it needs to be unveiled more and more as we have done with smoking.

Senator Schmitt. Is there anything in the revolution of understanding of biomechanisms, natural biomechanisms, that give us some insight on how we can anticipate a susceptibility to alcoholism on the one hand and maybe provide an antidote to alcohol poisoning, if I may use that term, as it affects the driver of an automobile?

Dr. Malone. I am not personally familiar with the scientific details, although I know that the NIAAA is working on the biochemistry of what happens when alcohol is consumed.

Senator Schmitt. Is it conceivable that there could be an antidote for alcohol?

Dr. RALL. It is not very conceivable because alcohol is metabolized in a fairly normal way with alcohol dehydrogenase, so that the body's enzymes recognize alcohol in perfectly reasonable things.

In answer to one of your earlier questions, there are some sociologic and psychiatric data which suggest there may be a genetic predisposition toward alcoholism. The researchers at the National Institute of Alcohol and Alcohol Abuse are concerned as to whether there might be some metabolites, such as methanol, which might show up unusually in people who are alcoholics. These data are in large part unpublished as yet.

IMPACT OF BUDGET POLICIES

Senator SCHMITT. Dr. Malone, the budget proposes to cap, as you indicated, indirect costs for research grants at 90 percent of actual cost, and also to reduce the average cost of noncompeting continuation grants by 3 to 4 percent, and to maintain training allowances slightly below the fiscal 1982 level.

What impact do you see that these policies will have on your research and training efforts?

Dr. MALONE. For fiscal 1983 we will have reduced capacity in funding investigator-initiated research. Nevertheless, we have been able to accomplish the level of support that we have projected only by effecting reductions across program lines.

We feel that we must reduce the indirect cost allowance as a fair share of the budget reduction during these austere times. Although we have done that, and although we will have some reduction in the number of projects to be supported, those competing research project grants that will be supported will experience an 8-percent increase in average cost and the noncompeting continuation projects will have a 5-percent increase.

Thus, those projects that we are able to support, which we think we are supporting at a level that will continue the momentum of this biological revolution, are being supported well and will allow the investigators to pursue their projects in full force.

Senator SCHMITT. What do you expect the number of grants to be under this plan?

Dr. MALONE. We expect to support 4,100 new and competing awards; including noncompeting awards, the total number of research project grants that will be supported will be about 15,000.

Senator SCHMITT. So we are a long way from the goal we tried to set a year ago, and that is 5,000 grants as a minimum sustaining base for the National Institutes of Health.

Dr. MALONE. Yes; we are some distance from that, but we feel that if we had reached for that goal this year—and we consider this as a temporary retrenchment—we would have done serious damage to the other components of research—the contracts, the centers, the clinical trials, and the like. What we are trying to do is to support an adequate number but at the same time to provide a balance of support for the other mechanisms.

Dr. Raub is the Associate Director for Research and Training. This is his bailiwick. I wonder if he might not like to add some comments to this point.

Senator SCHMITT. Dr. Raub.

Dr. RAUB. The main area, let me elaborate briefly, is in the consequences for awardee institutions. We have described the general impact on the programs of these various reductions. For the indirect cost cap, one of the effects will be for us and the university community to examine better means to establish greater discipline over these costs which are real and important but nevertheless difficult for both of us to justify, and something that we would rather not continue to increase as a fraction of the total awards. We have a good deal of work to do with the university community on finding better means to deal with those kinds of costs.

PRIVATE SECTOR SUPPORT

Senator SCHMITT. Do you see any increase in private resources to assist in making up the difference?

Dr. MALONE. This is an issue of concern that we have had under very serious consideration for the last 2 years. It is a matter that has been discussed at length by the Director's advisory committee, and we have brought together members of industry, from the university, and the Government sector.

We see no immediate help from industry. Industry a decade ago was providing about 3 percent of research support to universities. Even though industry provides more money today than in 1971, it is about the same percentage. So we see no immediate relief from this source. After all, the trend for this support is relegated to their own purposes, to drug development, to pharmaceuticals, and so forth, and is not always consonant with the purposes of basic research.

Nonetheless, we have been meeting with industry representatives to try to find ways of providing some relief but, quite frankly, I see nothing in the future that presumes that we will receive significant aid from industry in this regard.

Senator SCHMITT. Well, we changed the Tax Code last year. Are you saying that will have no effect?

Dr. MALONE. The tax structure, you say?

Senator SCHMITT. The Tax Code was changed last year to provide greater incentives for contributions to university research environment.

Dr. MALONE. We have not yet begun to see the results of that Tax Code. We know that a few industrial organizations have made contributions to a few institutions. One can count them on one hand—Harvard, MIT, and a few others. We have looked very closely at these arrangements. There are some gains and pluses in such arrangements, such as who has patent rights, what does the contributing industrial organization want to exact out of such an arrangement. We are looking at the implications of all this for other studies that might receive support from industry.

CHANGES IN PATENT LAW

Senator SCHMITT. Are you examining the effects of the changing patent policy relative to universities and small businesses?

Dr. MALONE. Yes, we are.

Senator SCHMITT. Does that represent a new source of capital for research, the retaining of patent rights by the contracting institution?

Dr. MALONE. Yes; we have established three working groups in the Director's advisory committee. One of these deals with cooperative relationships with industry. That working group has, over the past year, examined the patent amendments very closely. We have examined the law and its implications, and intend to issue some guidelines to the institutions. It is our opinion that the more liberal attitude in giving patent rights to institutions and small businesses will perhaps allow them to realize some profits, but it is actually too early to predict what the impact of those amendments will be.

RETENTION OF SCIENTISTS

Senator SCHMITT. Does the situation exist in bioscience and bioengineering that exists in other science and engineering, where industry principally is moving in to hire the best undergraduate baccalaureate degree-holders out of the advanced-degree stream, and also hiring away the best of their professors? Is that happening in this field also?

Dr. MALONE. Yes; we have seen some movement. I do not think it is a level that presents a problem for us at this time, but as industry expands, I think we can see that they will attract more and more scientists, particularly——

Senator SCHMITT. But this is a self-defeating effort on their part and really represents a divergent situation within education of the raw material for science and technology within industry. If they are short of advanced degree-holders but at the same time they are doing relatively little to keep the students who should move on into graduate school in that stream, educational stream, and to provide support for professors, who would teach them? It's happening all through science and technology, and I'm just wondering how serious the problem is in the biosciences.

Dr. MALONE. There appears to be a slight drain on the attraction of Ph. D.'s—not at the undergraduate level. It is a problem that we are looking at and are paying very close attention. In our dialog with the industrial representatives, one of the areas we intend to discuss is any modality by which industry might contribute to the training of researchers and, therefore, contribute their fair share of that process.

Senator SCHMITT. Well, if they had any perspective at all on what is going to be essential for their future survival within an industry, they would be investing in the creation of the raw material people to the same level they invest in the maintenance of a stable supply of raw materials of other kinds that they need in their industry.

I find it extraordinary that we have seen so little movement by industry to move forward to not only fill the gap that is having to be left by Government assistance—temporarily I hope—but to take care of the basic underlying shortfall of training people that everybody knows exists and is being created in part by this extreme competition for the best and brightest out of the universities.

Dr. MALONE. Yes, I agree.

Senator SCHMITT. I am going to have to go vote. We will recess for about 10 minutes.

[A brief recess was taken.]

IMPACT OF 1982 CONTINUING RESOLUTION

Senator SCHMITT. Let's continue.

Dr. Malone, what has been the impact of the 1982 continuing resolution which imposed the lower of the House and Senate figures and the 4-percent reduction on top of that?

Dr. MALONE. That impact has, of course, reduced the overall budget outlay from $3.8 to $3.64 billion. Under the terms of the continuing resolution, this must be further reduced by $7.4 million for reductions in salaries and other expenses. The 4-percent reduction within that framework will still allow us to support almost 4,800 research grants—only a modest impact there. We will have a 4-percent reduction in training dollars and will, therefore, support nearly 500 fewer trainees under the continuing resolution. We are continuing to provide approximately 50 percent of the institutional allowances, so there will be that measure of impact on research training.

In other research mechanisms, we will be able to initiate very little new activity in research centers and R. & D. contracts. We will not be able to mount all the clinical trials that we would like. Indeed, of the nine additional ones we specified earlier, we will be able to support only two—one at the level of a pilot study and the other a feasibility study.

Intramural research will similarly suffer in that, although it would appear that it has only a 2-percent reduction, we will absorb the October 1981 pay raise; therefore, the actual reduction is about 4 percent.

Across the board we see this sort of impact with all our programs; however, with the kind of planning that has been suggested by the institutes in the selection of clear priorities, we will at least be able to continue the momentum within the framework of the 1982 continuing resolution level.

INFLATION RATE

Senator SCHMITT. What inflation rate do you project, and what have you experienced in the past budget year?

Dr. MALONE. The biomedical research inflation rate is about 8.2 percent for 1982; and for 1983 it should be perhaps 6.5 percent or a bit more. Mr. Mansfield, this inflation rate is a bit higher than what we would expect to see for other commodities. You might want to comment on that.

Mr. MANSFIELD. There is a distinction between the cost of salaries, which are controlled on the Federal level and probably have not been going up as rapidly in the extramural institutions as the inflation rate in general. However, there have been extremely high increases in the cost of equipment, supplies, and other materials that are used in research. The assumption in the President's budget for 1983 is, as Dr. Malone said, 6.5 percent.

DIRECT OPERATIONS AND PROGRAM MANAGEMENT

Senator SCHMITT. Have you undertaken a study of savings that can be achieved in direct operations and program management, Dr. Malone?

Dr. MALONE. We do not have an ongoing study as such, but we can point to a number of areas where we have tightened our own belts. In the first instance, it has been done for us by the budget itself, which limits our capacity for making new and competing awards. Our review process identifies the very best science that can be supported; in this way we are making some definitive priorities about the nature of science that is being supported.

The administrators of the extramural programs are reducing costs in such areas as travel and in the performance of site visits. I have already indicated that we are not making new starts in several areas.

All our Institutes are making very careful analyses of their programs and making economies wherever possible. I do not want to preempt Dr. DeVita, but I hope he talks about the excellent progress that he has made in this area, which is typical of what is going on in other Institutes. He will perhaps describe what he has done to centralize decisionmaking in the Cancer Institute. He has analyzed the Institute's approximately 1,100 contracts covering the last 2 years and has eliminated or reduced many of those to the tune of about $40 million, and he has reorganized programs making premium use of people and resources. I expect you will find that this kind of approach is going on in all our programs.

In the intramural side of the house, there are many indices of what is occurring. Dr. Rall tells me they have had very few new hires over the past year; they have bought no new equipment without increased justification; they have had a decided reduction in travel; they are making a careful analysis of all orders for supplies to make the most efficient use of that budgetary item; they have reevaluated such things as computer costs; and they have cut back considerably on overtime.

Therefore, I can assure you that, in all our programs, both extramurally and intramurally, we are attempting to make the most efficient use of the funds available to us.

DISTRIBUTION OF REDUCTIONS TO GRANTEES

Senator SCHMITT. Have you noted that in the reduction of grants and training assistance there is an equal distribution of that burden of cuts between large and small institutions? Or are the small institutions, with maybe less political weight in the peer review system, suffering more than the large institutions?

Dr. MALONE. I am absolutely certain that when our Institutes make reductions they do it on a project-by-project basis and not with respect to the host institution.

It is clear that there are some differentials in where the grants are. A good many grants are in the larger institutions where there has been an attraction for the best investigators, but when it comes to the matter of exercising these cuts that we are imposing, it is done across the board and as objectively as possible.

Senator SCHMITT. Do you feel that the representation within the peer groups is sufficiently broad that there would not be any bias toward the larger institutions?

Dr. MALONE. I am quite certain of that. Such an impression might arise from the fact that the larger institutions receive most of the funds, and they have been able to attract the best scientists. Therefore, since we are concerned with the support of quality research, one would expect to see that kind of differential.

We have done everything possible to assure fair representation on our advisory bodies. Indeed, the last study that was conducted on our peer review system was in-house. A study team chaired by Dr. Kirschstein made recommendations, which have been implemented, to advertise the vacant slots and make the vacancy lists available to everyone. We have, in the last decade, made an outstanding series of steps in making advisory committee positions available to minorities and women. Indeed, if one looks at just one index, in 1972 we had 12 percent females on our advisory bodies. Now we are approaching 25 percent. We have similar data for blacks, Hispanics, and other minorities.

I believe that the system is fair. It has been reviewed more than any other system that I know of, more than a dozen times, and each time there has been improvement. The peer review system has its own built-in checks and balances, so I think the results of the system are fair and equitable.

As a final statement, I think if one looks at the hundreds of thousands of projects we have supported over the years, certainly since World War II, the peer review system has been one that has been quite satisfactory to those who have received the awards and to those who have been disapproved. The number who disagree with the system are an infinitesimally small percentage.

DIABETES INITIATIVE

Senator SCHMITT. Thank you, Doctor.

In our 1982 committee report, we noted you have been conducting a multi-Institute diabetes initiative for the past 5 years. I think it's safe to say that the committee overall expects that you will pursue this initiative. Do you feel it has been worthwhile and is worth pursuing?

Dr. MALONE. Yes; I think this has been one of the most successful of the trans-NIH efforts. It has been spearheaded by Dr. Salans, the head of our diabetes program at NIH. Many of our Institutes contribute to this effort. It allows for the exchange of information; it avoids duplication; and it has led the attack on problems with each Institute contributing from its own particular research base. I think it has been exceedingly successful, and I expect Dr. Salans will give you more specifics about this activity.

TRANS-NIH ISSUES

Senator SCHMITT. How many such multidisciplinary, multi-Institute efforts do you have underway in a semiorganized fashion?

Dr. MALONE. In addition to diabetes, we have a very effective nutrition program with a nutrition coordinating committee chaired by Dr. Simopoulos. We have a new NIH-wide program in prevention. Others include arthritis, cystic fibrosis, and manpower development. These programs represent a very positive effort and also a more efficient use of resources at NIH.

TECHNOLOGY TRANSFER

Senator SCHMITT. The committee's report also noted its interest in NIH making certain that new or emerging research technology is pushed to the point where its commercial potential can be fully evaluated.

Is this effort worthwhile and is it continuing and can it continue in light of the budgetary restraints?

Dr. MALONE. Yes; I think that this is an extremely important initiative. We do indeed want to move across the spectrum of activities from basic research to technology transfer. Some years ago, Dr. Fredrickson created the Office for Medical Applications of Research. That office has the responsibility for fostering the development of new technologies and their transfer, as well as the review of old technologies that have been in existence for some time. We are devoting about 5 percent of our budget to this effort; we see this as an important entity and would expect to see it increasing and improving over the years ahead.

PROSTAGLANDINS

Senator SCHMITT. Doctor, one final question. It may be coincidence; it may be I haven't been doing my reading, but I noted, as I recall, about a year ago, a great deal of interest in prostaglandins in a broad way across several Institutes. Has that interest died down? Has something happened that has kept me from reading more about it, or am I just negligent in my reading?

Dr. MALONE. I think that the interest is as high as ever.

Senator SCHMITT. Maybe when one of the appropriate Institutes come forward, they can summarize it.

Dr. MALONE. Yes: we can see that someone speaks to that.

Senator SCHMITT. And also I have heard more recently about monoclonal antibodies than I have about prostaglandins. Maybe they could also speak to that.

Dr. MALONE. We will see that someone speaks to it.

SUBMITTED QUESTIONS

Senator SCHMITT. Thank you, Doctor. We will move on to the individual Institutes. We appreciate it very much. Of course, there will be other questions for the record.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

BUDGET POLICY

Question: We hear that the new budget provides for funding only about 30 percent of approved research grants. What can you tell us about this -- and how does it compare to fiscal 1982? Fiscal 1981?

Answer: The NIH continues to place high priority on investigator-initiated research, with almost 50% of the total resources requested in 1983 devoted to research project grants. This is the same percentage of total NIH resources as this mechanism received in 1981 and in 1982 under the current Continuing Resolution. It should also be noted that the 50% allocation to research project grants in recent years is a substantial increase over past allocations; for example, as recently as 1978, research project grants represented 40% of total NIH resources.

We are, however, experiencing a decline in the award rate for new and competing research project grants. In 1981, the award rate was 39%, compared to an estimated 32% in 1982 and 27% in 1983. This decline in the award rate can be attributed to several factors: 1) the number of grant applications being received is increasing each year; consequently, even if we funded the same number of grants each year, the award rate itself would decrease; 2) the average cost of each research project grant is increasing each year because of the increased cost of conducting research; and 3) in order to support on-going commitments in research project grants, a decreasing dollar amount is available for new and competing grants.

REDUCTIONS IN NEW GRANTS

Question: The budget proposes an increase of $109 million for NIH in FY 1983, yet you propose to reduce the number of new funded research grants by more than 600. Please explain this seeming inconsistency.

Answer: Approximately 4,100 new and competing research project grants will be funded in the 1983 budget request, a decrease of 641 from the 1982 level of 4,741. The budget continues to place priority on research project grants, but recognizes that support for the other programs should not erode further as a proportion of the budget. Other support mechanisms are essential for translating the results of basic research into treatment and disease prevention and for developing crucial research expertise and research resources to continue the momentum of American medical science. Accordingly, the proportion of the 1983 budget devoted to new and continuing research project grants has been maintained at 50 percent, the same level as in 1981 and 1982.

Question: Why does the number of noncompeting project grants and administrative supplementals go up?

Answer: In 1983, the number of noncompeting continuation research project grants will increase by 67. There will be 11,041 grants of this type in 1983 as compared to 10,974 in 1982. The number of noncompeting and administrative supplemental grants in a particular year is a function of the number and type of awards made in prior years.

COST-EFFECTIVENESS

Question: We hear much talk about the cost-effectiveness of biomedical research. What can you tell us about this?

Answer: Anyone over 50 years of age has lived to see--and in many cases to be vitally affected by--the discovery and development of the antibotics, the substitution of the polio vaccine for the iron lung, the widespread use of non-invasive techniques that have made diagnostic surgery unnecessary, and a host of other recent benefits of biomedical research.

Considered only in terms of dollars, benefits to the economy from biomedical research have been estimated at 10 to 16 times the cost of the research. Perhaps more important, however, are the benefits that accrue from improved health and quality of life for the American people.

Question: How can you prove the statement in your justification that "for every dollar invested in biomedical research, 13 dollars has been returned to the economy in terms of longer life and reduced illness."

Answer: The quotation you have cited was derived from a study conducted by Dr. Selma J. Mushkin of Georgetown University. In her book Biomedical Research: Costs and Benefits (1979), the model she applied to examine the impact of biomedical advances considers the reduction of mortality and morbidity against such factors as income levels, environmental hazards, social stress and the provision of health care.

Dr. Mushkin attributed the reduction in deaths and sickness to new medical knowledge and new therapies gained through biomedical research. She quantified the value of the reduction in premature death and in work time loss due to sickness, and analyzed the shares of these values attributable to biomedical research. The value of each death averted was estimated at $76,000, and the value of a work year of sickness averted was estimated at $12,250. Mushkin and her colleagues concluded that 30% to 40% of the mortality reduction and about 39% of the reduction in the objective sickness rate were attributable to biomedical research. Benefits to the economy from biomedical research were found to be 10 to 16 times the cost of the research during the period 1900-1975, resulting in a net savings of $227 to $407 billion. Therefore, conservatively speaking, for every dollar invested in biomedical research, the economy indeed receives a return of 13 dollars.

ACHIEVEMENTS

Question: Each year it has been the practice of NIH to review major achievements and breakthroughs in biomedical research. Please summarize major achievements and breakthroughs in NIH-sponsored biomedical research over the past year.

Answer: We have been witness to an extraordinary period of scientific opportunity and advancement in biomedical research. Some recent examples of these achievements follow:

Immunology and Virology: The emergence of powerful recombinant DNA and hybridoma (cell fusion) technologies, coupled with an increased understanding of the immune system, now permits radically different approaches to the many still unresolved problems of immunology. Among the important advances that have been made are the following:

- During the past year, clinical trials, some of which were conducted by NIH, demonstrated the efficacy and safety of a hepatitis B vaccine. The vaccine has now been licensed by the Food and Drug Administration. Immunization programs based on this success may ultimately not only reduce the incidence of acute hepatitis B, but also may reduce morbidity and mortality from chronic active hepatitis, cirrhosis of the liver, and cancer of the liver.

- Investigators have developed a convenient, low-cost test to screen newborns for cytomegalovirus (CMV). This virus is frequently transmitted to infants at or near the time of delivery and is believed to be a leading cause of hearing impairment. It is also a cause of serious infection following kidney transplantation.

- Hybridoma research is being exploited to permit the detection of cancer at a very early stage by allowing scientists to label cancer cells in the body. The high specificity of the monoclonal antibodies produced by hybridoma techniques may lead to the killing of cancer cells by means of chemotherapeutic agents attached to the antibodies that specifically seek out and bind to cancer cells.

- In vision research, scientists have shown that some cases of uveitis (inflammation of the inner eye) may be triggered by exposure of the immune system to a certain enzyme protein present in all normal eyes. Investigators have now tested various drug treatments in animals and have found that cyclosporin A, a drug currently used to prevent transplant rejection, can prevent the disease in laboratory animals.

Genetics and Gene Regulation: Recent discoveries have increased our understanding of the way genetic information is encoded and transmitted. Researchers are beginning to identify the fundamental defects in specific genetic diseases and to search for methods to repair them.

- One exciting research advance concerns transposable genetic elements. New knowledge has been gained regarding the ability of portions of chromosomes to rearrange themselves. It is this process that is responsible for the diversity of antibodies. Another area of accomplishment is that of genetic regulation--the process by which cells control the production of cell components. An important recent development has been the discovery that cell transformation in vitro by retroviruses is frequently due to activation of one or two normal genes of a normal cell by the virus. Transformation in vitro is generally considered to be similar to the change from normal cells to malignant or cancerous cells. Retroviruses are relatively common RNA viruses found throughout nature.

- Knowledge of how environmental chemicals influence the mobile elements of DNA to determine the expression of damage, mutation, and heritable disease is advancing rapidly. A major initiative is aimed at improving short-term tests that measure the genetic and cellular changes thought to be precursors of carcinogenesis.

Noninvasive Diagnostic Techniques:

- Positron emission transaxial tomography (PETT)--a computer assisted imaging technique that enables visual mapping of metabolic processes of the brain--is now being applied experimentally to the fields of psychiatry, neurology, and gerontology. Current and potential uses include studies of schizophrenic patients, and the study of electroshock therapy, Alzheimer's disease and epilepsy.

- An even newer, and potentially safer, noninvasive imaging technique, utilizing the principle of nuclear magnetic resonance, is being developed in the NIH intramural program.

Receptor Site Defects: Researchers have recently postulated a unifying concept for explaining the mode of action of a wide range of biologically active substances. Receptor sites on cell membranes are seen as "locks" into which a bio-active "key" fits in a highly specific manner to initiate a response.

- As part of this research, scientists have learned that the development of diabetes in certain patients appears to be due to a deficiency in the "insulin receptors" which enable the body to respond to the insulin by lowering blood sugar level. Similar deficiencies have been noted in other diseases as well, including myasthenia gravis and disorders in calcium and bone metabolism caused by nonresponse to vitamin D.

- The receptor site concept has been especially fruitful in neurobiology including the study of endorphins--the body's own pain killers. This research is providing a fuller understanding of the mechanisms of brain function, the causes of drug abuse, and the treatment of pain.

Prevention: Disease prevention continued to receive special attention in our planning and allocation of resources. In 1981 well over one-half billion dollars was spent on research directly related to prevention. Notable past successes have been achieved by strategies built on knowledge and technology provided by NIH research -- the high blood pressure control program and other programs to reduce the risk of heart attack and stroke being examples. The National Toxicology Program is another example of an outstanding prevention activity. Progress is being made in many other areas, including the following:

- The prevention of some types of cancer may be possible through administration of naturally occurring or synthetic organic chemicals that appear to promote or inhibit cancers. Through epidemiological and experimental research, these substances and their effects are being identified, dose responses determined, and plans considered for clinical trials. Diet and nutrition research is also part of this effort.

- A recent survey has shown that the prevalence of dental caries is about 30 percent lower than it was at the time of a 1971 survey. This reduction is attributed in large part to more widespread availability and use of fluorides, a longstanding initiative of the NIH.

- Progress is being made on vaccines other than hapatitis B. A live attenuated varicella vaccine appears to have promise for prevention of the serious and often fatal infections that leukemic children develop when exposed to chickenpox.

- Antiviral drugs are now the best hope of preventing influenza A during epidemics and the recurrence of herpesvirus infections in patients receiving immunosuppressive therapy.

- Work on the prevention of asthma and allergic diseases, particularly those associated with occupations, is progressing. Methods to induce blocking antibodies or tolerance to specific allergens appear promising, as does work with chemically modified allergens to improve immunotherapy.

- Clinical trials are underway to learn whether vitamin E therapy in premature infants will reduce the risk of retinal damage and blindness. Other work is directed at senile cataracts since it appears quite possible that these are due to long-term oxidative damage, possibly triggered by exposure to light in the environment. If so, methods of protection can be devised.

- Low density lipoprotein (LDL) is the major vehicle for transporting cholesterol in human blood plasma. The mechanism for degrading LDL has now been demonstrated in animals, and may eventually lead to clinical applications to control cholesterol levels in the blood stream and thus to contributing to the prevention of heart attack.

Question: Where do we stand on conquest of the immune system? On interferon?

Answer: In experimental animal models manipulation of the immune system has been shown to be possible, and translation of these techniques into humans is progressing. For example, children with a congenital absence of immune system factors can be immunologically reconstituted through transplantation of cells from the thymus.

The availability of pure (monoclonal) antibodies generated from hybridomas is permitting a new approach to the treatment of acute lymphoblastic leukemia of childhood. The approach is the selection killing of cancer cells by treatment with hybridoma antibodies directed against cell-surface antigens unique to the cancer cells. Through this type of treatment, abnormal cells only are the target of the attack.

We now have the ability to modify the internal processes that regulate the immune system. Such knowledge has been used to improve the results of kidney transplants. It is possible, for example, in the immediate post-transplantation period to detect the rejection process at the very onset. As a consequence, with appropriate early treatment the rejection of the transplant can be prevented.

From the new knowledge on the immune system, experimental treatments can be designed for the effective management of patients with immunologic diseases (such as systemic lupus erythematosus and rheumatoid arthritis) characterized by the oversuppression or overstimulation of the immune system.

The interferons are a group of biological substances that appear to have some anticancer activity. Since there are several different types of interferon and within each type there may be several different molecular species of interferon, the usefulness of this family of biologics will require extensive testing. The National Cancer Institute is currently completing Phase I trials to determine the tolerated dose and toxicity of several interferon preparations and has determined that some of these interferon preparations can be given at higher doses than was originally predicted. The side effects have been quite predictable and appear to be self-limited. There have been some tumors which have responded to treatment, and these responses are of great interest from a therapeutic point of view. Most of the responses have been partial (the tumor has not completely disappeared) and have been of short duration (a few months). However, any biologic that has anticancer activity is of interest. Current approaches are to confirm and extend these observations in Phase II trials to determine which cancers are most responsive to the interferons. Following would be Phase III trials, where interferon preparations are tested in conjunction with standard anticancer treatment to see if additive efforts could be detected. It is not currently anticipated that the interferons will substitute for or eliminate the need for other anticancer therapy in any particular malignancy. However, it is hoped that the interferons, being a different class of substances with different types of toxicities, might be additive and useful in the multimodality treatment of cancer. It may be several years before the exact role of these interferon preparations can be determined with respect to integration with other forms of cancer therapy.

PROTECTING PROGRAMS

Question: Which programs in the NIH at large do you feel offer the greatest promise of breakthrough and therefore should be maintained at present or increased levels of funding?

Answer: Scientific breakthroughs are not easy to predict since research is essentially a continuing process of discovery in which today's assumptions or theories can be modified by tomorrow's findings. A number of areas of investigation, however, show promise for substantial contribution to biomedical knowledge or medical treatment and consequently deserve high priority. Examples of these promising areas include:

- Studies of the chemopreventive properties of retinoids (vitamin A - related compounds) in populations at high risk of cancer.

- Research into viruses associated with cancer. Last year a landmark discovery was made when a virus associated with leukemia was isolated. Now that the cause of this particular form of cancer is understood, much work can be done toward prevention.

- Heart and vascular disease. A new group of pharmacological agents, which block the passage of calcium across cell membranes, shows great promise for the control of abnormal heart rhythms, angina pectoris, and other coronary problems.

- Diabetes research. Recent developments, such as synthetic production of human insulin using recombinant DNA techniques and transplantation of the insulin-producing cells of the pancreas, have contributed much momentum to the study of this disease. Considerable potential exists for further advances in the day-to-day treatment of diabetes.

- Studies of the nervous system. As a result of recent findings in neurochemistry and neurobiology and the use of non-invasive imaging techniques, science is on the threshold of knowing how the nervous system functions as the master regulator and coordinator of most body functions. Such knowledge has significant implications for the prevention and treatment of neurological disorders.

- New vaccines utilizing recombinant DNA and hybridoma technologies, including a second generation hepatitis B vaccine, and vaccines for sexually transmitted diseases, infant diarrhea, dental caries, and bacterial meningitis.

- Genetic research, in which recent discoveries about the moveable segments of the DNA molecule show great promise in understanding how the immune system works, and why cells age and die or why they become malignant in response to environmental factors.

- Prevention or alleviation of birth defects by means of emerging techniques such as fetal surgery, drugs that inhibit premature birth, and screening tests for inborn errors of metabolism.

- Clinical studies toward prevention of diabetic retinopathy and senile cataracts.

Question: Can you identify those programs you feel should be expanded?

Answer: The list of high priority activities provided above indicates a broad range of important and promising research being supported by NIH. It would be difficult to judge some activities as being of greater merit than others because each of them holds a significant potential for better health and an enhanced quality of life. It would be desirable, given additional resources, to expand nearly all these activities because the pay-off to the American people would be brought that must closer to realization. The promise inherent in these areas of research must be weighed, however, against the current constraints in Federal spending and the need to maintain an overall programmatic balance among the types of research that NIH supports. Because it is so difficult to predict where breakthroughs may occur, we believe it is necessary to move forward on a broad front and not prematurely terminate potential avenues of success.

Question: Can you identify any areas in biomedical research where new program initiatives are needed?

Answer: New research initiatives emerge from the opportunities and promise created by significant discoveries. For example, the emergence of powerful recombinant DNA and hybridoma (cell fusion) technologies coupled with an increased understanding of the immune system now permits radically different approaches to the many still unresolved problems of immunization. The 1983 budget request addresses this and other significant opportunities such as genetic research, fetal surgery, and non-invasive imaging techniques, to mention but a few. Investigator-initiated research continues to represent the primary mechanism for discovery of such new opportunities. We are confident that, through the peer review system and NIH in-house scientific expertise, the most crucial research initiatives are properly identified and supported.

Question: What impact did the Omnibus Reconciliation Act have on NIH programs this year?

Answer: The Omnibus Reconcilation Act of 1981 had impact for NIH in two areas. First, the Act provided reauthorization of the National Research Service Awards program for 2 years at the following levels: $182,000,000 in 1982, and $195,000,000 in 1983. For 1982 this represents a reduction of $40,500,000 from the 1981 authorization level of $222,500,000. This authority is shared by NIH with the Alcohol, Drug Abuse and Mental Health Administration. Under the reduced authorization level for 1982, approximately the same number of trainees could be supported as in 1981, but with approximately a 50-percent reduction in the level for institutional allowances.

The second area affected is the Assistance to Medical Libraries program of the National Library of Medicine. The program was reauthorized for one year at a level of $7,500,000 for 1982, compared to the 1981 authorization level of $18,500,000. The budget for this program was $9,831,000 in 1981 compared to the 1982 authorization level of $7,500,000.

CUTTING BACK PROGRAMS

Question: Can you identify specific programs in NIH that can be significantly cut back or eliminated entirely? Can you categorically and by priority target those programs you feel are most amenable to trimming back without jeopardizing research and development progress? Which categorical programs could be eliminated entirely with a minimum impact on public health?

Answer: It is not possible to know precisely where the next important medical breakthrough will occur. To significantly cut back or eliminate any of the specific or categorical programs at NIH would slow progress toward improved health of the American people and containment of health care costs through new prevention or treatment measures. It should also be noted that the NIH operates with a built-in regulator; i.e., scientists do not proceed with research that they and their peers believe has little chance of success.

INFLATION/EXTRAMURAL COSTS

Question: How has inflation affected the buying power of the research dollar over the past 5 years?

Answer: Biomedical research costs have been affected by inflation over the last 5 years. From 1976 through 1981, the funds required to support a fixed level of research and development have increased by about 50 percent, as measured by the Biomedical R&D Price Index. In other words, $1.5 million at 1981 prices would be the equivalent of $1.0 million at 1976 prices in biomedical R&D purchasing power.

Question: Likewise, what has been the trend in extramural overhead costs during the same period?

Answer: During this same period, the indirect cost rate on research grants has increased from 26.7 percent of total costs in 1976 to 29.5 percent in 1981. While the indirect cost rate reflects a 3 percent change from 1976 to 1981, the base (total cost) used for calculating the rate has increased significantly, therefore resulting in a considerable increase in indirect costs.

INFORMATION DISSEMINATION

Question: What new initiatives have been implemented during the last year to improve the dissemination of timely information to the public?

Answer: In addition to continuing a wide variety of public information programs, including regular news feature services, close collaboration with reporters and science writers from the major media, and responses to nearly half a million public inquiries, components of the NIH during the past year have concentrated on cooperative activities designed to provide new channels for dissemination of information. For example:

- The National Institute on Aging (NIA) initiated a collaborative program with Peoples Drug Stores, Inc., aimed at providing the elderly and their families with important health information developed by the NIA. Brochures on topics of importance to the elderly have been made available at Peoples' expense in all Peoples' 525 stores in 15 states and the District of Columbia.

- The National Heart, Lung, and Blood Institute (NHLBI), in addition to carrying on its health promotion activities in the areas of smoking cessation, and high blood pressure control (through life insurance companies, business and industry, unions, and voluntary business and health associations), is encouraging organizations to plan programs at their own expense based on information from an NHLBI publication, Exercise and Your Heart--a publication which explains how to safely begin and maintain an exercise program for maximum cardiovascular benefit. Good Housekeeping magazine this year reprinted major portions of the booklet, thereby reaching more than 9.5 million readers.

- The National Cancer Institute (NCI) has continued to carry out its large scale education/information programs on smoking prevention and cessation, breast cancer education, and "coping with cancer" (designed to help cancer patients and their families gain a sense of control over their lives by providing them with information on the disease, its treatment, and psychosocial aspect). Emphasis is on setting up new collaborations with non-government intermediaries, such as professionals, businesses, unions, and civic organizations, which in turn convey the information to segments of the public.

- The NIH has increased its efforts this year to disseminate information to the public on disease prevention and health promotion. This is done by providing timely, scientifically accurate information to writers, editors, syndicated health columnists, and others who can reach large numbers of individuals through their articles in newspaper and magazines.

- The NIH has refocused its program of Science Writers' Seminars this year to be more clinically oriented. These seminars are held to provide science writers and editors with background information on ongoing areas of research where advances are expected to emerge. The newer focus on clinical topics should lead to more and better coverage in the major communications media of topics with direct relevance to the public health.

- This year NIH has expanded its long-standing working relationships with general magazines to include the new, so-called "lifestyle magazines" (such as Self, Vogue, and Glamour). These magazines, with their large leaderships and great interest in health topics, have come to rely upon NIH for story ideas, for scientific background and professional contacts on particular stories, and for fact checking to assure scientific accuracy.

- The Office for Medical Applications of Research, the organization at NIH responsible for overall coordination of technology evaluation and technology dissemination has continued to sponsor a number of consensus development conferences and has initiated a number of studies to improve on its ability to meet its obligations.

Question: What are consensus development conferences, how do you use them and how much do they cost?

Answer: NIH Consensus Development Conferences bring together biomedical research scientists, practicing physicians, consumers, and others in an effort to reach general agreement as to whether a given medical technology is safe and effective. The consensus process represents a special kind of technology assessment as a preliminary step before technology transfer. The consensus conferences seek to resolve important issues surrounding emerging as well as established technologies. Each consensus development conference costs approximately $55,000 to $65,000.

Question: What consensus conferences are you planning for the coming year?

Answer: The following conferences have been scheduled:

	FY 1982
CT Scanning of the Brain	Nov. 4-6, 1981
The Effect of Diet on Hyperactivity	Jan. 14-15, 1982
Hip Joint Replacement	March 1-3, 1982
	FY 1983
Immunotherapy - Treatment of Insect Sting Allergy	Oct. 1982
Clinical Applications of Biomaterials	Nov. 1-3, 1982
Issues Related to the Utilization of Intensive Care Units (ICUs)	Dec. 6-8, 1982

Additional conferences are under consideration:

Computer-Based Hospital Medical Information Systems

Therapy of Hypertriglyceridemia

Utilization of Hepatitis-B Vaccine

Liver Transplantation

Question: Will any conferences have to be cancelled due to budget restrictions? Please specify.

Answer: No conferences have been cancelled as a result of budget limitations.

Question: Do you still use consultants to set up these conferences?

Answer: When appropriate, outside consultants who are expert in the subject technology are used by NIH to assist in planning consensus meetings. To date, consultants have participated in the planning associated with most conferences; in each case, only two to three consultants have been involved.

NIH DIABETES INITIATIVE

Question: In our 1982 committee report we noted that you have been conducting a multi-Institute diabetes initiative for about the past five years. What arrangements do you have for managing this cross-Institute activity to make certain there is no overlap and duplication?

Answer: We have established the NIH Diabetes Coordinating Committee to coordinate activities, exchange information, develop policies, engage in joint planning, and assess progress. The Committee is headed by the NIADDK Associate Director for Diabetes, Endocrinology, and Metabolic Diseases and is composed of representatives of all Bureaus, Institutes, and Divisions at NIH that have an active role in diabetes activities.

We have also established a Diabetes Mellitus Interagency Coordinating Committee. The NIADDK Associate Director for Diabetes, Endocrinology, and Metabolic Diseases serves as Chairman. The members are representatives from selected Institutes within the NIH that are active in diabetes, the Chief Medical Director of the Veterans Administration, a medical officer from the Department of Defense, and representatives of those other Federal departments and agencies whose programs involve diabetes. Through this Committee, we can coordinate activities, avoid overlaps, arrange for joint planning or action steps, and determine progress.

Question: What results are we getting from this initiative?

Answer: These coordinating committees have been most effective in avoiding any possibility of overlap or duplication. Their members share and discuss not only ongoing, diabetes-related research activities, but also compare plans for future activities and discuss promising directions of future research, obviating situations conducive to duplications or overlap.

Question: How much does NIH now spend overall on diabetes research--and how does this compare with previous years?

Answer: Obligations and estimated amounts for diabetes and related research supported by the NIH are the following:

1980 actual	$134,262,000
1981 actual	147,822,000
1982 estimate	151,607,000
1983 estimate	155,247,000

EMERGING TECHNOLOGIES

Question: In our fiscal 1982 report the Committee noted its interest in NIH making certain that new or emerging research technology is pushed to the point where its commercial potential can be fully evaluated. What arrangements do you have to make the private sector aware of your technological developments and to see if they have commercial possibilities?

Answer: As you know, last year Congress enacted patent and trademark amendments (P.L. 96-517) intended to spur the commercialization of inventions made with Federal funds. The new law provides small businesses and nonprofit organizations with the right to elect title to such inventions.

Interestingly, the law is consistent with previous NIH attempts to facilitate the transfer of inventions into commerce. To give universities a greater incentive to find or create markets for their research results, NIH -- and the Department in general -- has long permitted research institutions to enter into patent agreements and has assigned them ownership of patent rights when it appeared to be in the public interest and would lead to more rapid commercial use of the invention.

Of the DHHS portfolio of over 1,300 issued patents or patent-pending applications, over 700 have been assigned or waived through several different kinds of agreements. In addition, over 50 DHHS patents and patent applications have been assigned to the Commerce Department's National Technical Information Service, which selects those having promise of commercial application and serves as a licensing agent.

Our implementation of the new law is being guided by a Working Group on Cooperative Research Relationships with Industry, established within the NIH Director's Advisory Committee. During the past year, this Working Group has carefully reviewed statutory provisions, as well as interim final implementing regulations, and has made a variety of recommendations to the NIH with a view toward furthering the goals of the new patent policy. For example, the Working Group has recommended that NIH develop patent guidance for grantees elaborating statutory and regulatory requirements and encouraging grantees to exercise their option to elect title to inventions. Implementing the new patent policy is also a major consideration of the NIH Office for Medical Applications of Research, which is responsible for coordinating technology transfer activities.

Question: What positive results can you point to in such cooperative efforts?

Answer: We certainly agree with the objectives of the new patent law and think that greater commercialization of Federal research and development will benefit all segments of society.

Although it is too early to assess the effects of the new law, the feedback we have received to date from the biomedical research community is generally positive.

DIRECTOR'S ADVISORY COMMITTEE

Question: We understand that through the Director's Advisory Committee you get into the area of better cooperation among government, industry and the universities as it relates to biomedical research. Can you tell us more about this -- how is the Committee being used to address the concept of government-private sector cooperation?

Answer: In the spring of 1981, a Working Group on Cooperative Research Relationships with Industry was established within the Director's Advisory Committee. A major charge of this Working Group is to examine issues related to patent rights and to protection of proprietary information where there is a commingling of Government and industry funds at projects conducted at universities and nonprofit institutions. The Working Group has also been asked to consider standards and procedures at NIH for governing the peer review of proposals involving cooperative research arrangements with industry and to identify potential improvements in administrative requirements applicable to biomedical research funding.

Since it inception, the Working Group has largely focused on issues surrounding the new patent law, P.L. 96-517, which is intended to spur innovation and commercialization of research by providing small businesses, universities, and nonprofit organizations with the incentive of retaining patent rights to inventions they make under Federal funding agreements. Specifically, the Working Group is providing advice concerning how NIH may best implement the statute to promote industry sponsorship of academic research and to encourage NIH grantee institutions to exercise and capitalize on their patent rights under the new law.

Question: Do you reach out to the major business concerns -- as well as trade associations -- to determine their interests and how those interests might contribute to the role of NIH?

Answer: NIH has made extensive efforts to benefit from the corporate perspective regarding cooperative relationships among Government, universities, and industry. For example, meetings of the Director's Advisory Committee and its Working Groups have been informed by presentations made by officials of the Sterling-Winthrop Research Institute, Bristol-Meyers Company, Monsanto Company, Hybritech, Inc., Merck Sharp and Dohme, and Eli Lilly and Company. The Director's Advisory Committee has also specifically reviewed models of collaboration--such as the Exxon-MIT and Monsanto-Harvard arrangements--in an effort to gain insight with which to provide useful advice to NIH concerning the enhancement of university-industry relationships.

DRUG DEVELOPMENT

Question: The National Cancer Institute operates a drug development program for the purpose of identifying and developing drugs to treat some forms of cancers. In several cases, we understand, NCI incurred substantial costs for testing and developing compounds which were subsequently marketed as anti-cancer drugs by the pharmaceutical firms which held the patents on the compounds. Why doesn't NCI require some type of reimbursement from firms which successfully market drugs which the Institute tested for them?

Answer: The National Cancer Institute's drug development program has been established because of the need to develop new drugs and the absence of sufficient profit potential to encourage industry investment. Until the last few years, the sales of anti-cancer drugs and the profits, if any, have been so small that the question of reimbursement has never arisen.

The emergence of new drugs with significant sales records (e.g., adriamycin, cisplatin) now justifies raising the question of possible reimbursement. Discussions are ongoing among the NCI staff and the General Accounting Office concerning this issue.

Question: How much has NCI spent on this testing and development program in fiscal 1981 and how much will it spend in fiscal 1982 and 83?

Answer: During 1981, the NCI spent $52,646,000 on drug development, including preclinical costs and the costs of Phase I and II clinical studies. Comparable costs for 1982 and 1983 are estimated at $47,579,000 and $45,884,000 respectively.

Question: How much did the drug companies involved earn from NCI's work in fiscal 1981? In previous years?

Answer: Industry has never divulged the sales figures for specific drugs. However, in calendar year 1979, Arthur D. Little, Inc. estimated the sales of selected cancer chemotherapeutic agents. If one considers those drugs not originating in industry that were developed entirely or largely by NCI, the sales for 1979 were as follows:

BiCNU (Bristol Myers)	$1,500,000
CeeNU (Bristol Myers)	1,000,000
DTIC (Dome)	< 1,000,000
Platinol (Bristol Myers)	10,000,000
	≤ $13,500,000

If one includes all 21 drugs developed since the NCI program started, in which the NCI played a significant role, total sales for 1979 were approximately $90-95 million of the total cancer chemotherapeutic sales of $140 million. This $140 million figure represented about 1.5% of the total U.S ethical drug sales for 1979 of $9.6 billion. Sales figures for earlier years are not available. They would have been smaller, but the relationships are probably similar to 1979.

Question: Place in the record a list covering fiscal years 1979-1981 showing the compounds you tested and developed and how much was spent by the government in each case.

Answer: It is not possible to allocate precisely the costs of testing and development for each drug for which an Investigational New Drug Application (INDA) was filed over the period 1979-1981. However, an average cost has been developed which relates to the type of agent. A synthetic agent costs about $505,000 to develop preclinically, a fermentation product about $720,000, a plant product about $760,000. To each of these amounts must be added an average of $500,000 to cover the expense of conducting Phase I/II clinical trials. Listed below are drugs developed and entered into clinical trial by NCI for 1979-1981, by year, with the total estimated costs of preclinical and clinical testing:

FY 1979	Costs
Thymidine	$1,005,000
DON	1,005,000
Misonidazole	1,005,000
2'-Deoxycoformycin	1,220,000
AZQ	1,005,000
Acivicin	1,220,000
Anthracenedione	1,005,000
FY 1979 Total	$7,465,000

FY 1980	Costs
Aclacinomycin	$ 1,220,000
FY 1980 Total	$ 1,220,000

FY 1981	
Desmethylmisonidazole	$ 1,005,000
5-Methyltetrahydrohomofolate	1,005,000
WR2721	1,005,000
FY 1981 Total	$ 3,015,000

Since each drug requires several years to reach clinical trial, the estimated costs as shown cannot be allocated to a single fiscal year.

PROPOSED INCREASE IN GRANTS

Question: The HHS Assistant Secretary for Management and Budget recently was quoted as stating that the proposed increase for NIH will "provide for an 8% increase in the amount awarded for new grants, on the average, and a 5% increase in the amounts that provided for continuations." Can you explain what was meant by this statement?

Answer: For NIH as a whole, the 1983 budget request will provide for an 8-percent increase in the average cost of new and competing research project grants. The average cost of competing grants in 1982 is estimated at $111,300, compared to the 1983 estimate of $120,000. The budget will also provide for a 5-percent increase in the average cost of noncompeting continuation research project grants. The average cost of noncompeting grants in 1982 is estimated at $116,494, compared to the 1983 estimate of $122,300.

GENERAL POLICY

Question: In a new era of Federal funding austerity, it will become increasingly necessary to operate the NIH biomedical research establishment on a principle of maximum efficiency and minimum waste. What will be your policy on new program initiatives, eliminating duplication and streamlining existing programs?

Answer: The NIH philosophy on new program initiatives has historically been, and will continue to be, largely dependent on the direction that we are led by scientific discoveries. The 1983 budget request affords highest priority to investigator-initiated research project grants, the recognized point of breakthrough for many of these fundamental discoveries. As areas of particular research need are perceived by health professionals and the public, the NIH endeavors to spur required momentum by issuing requests for applications in these fields. In some cases, the Congress itself has provided the framework for new program initiatives. These times of funding austerity necessitate careful selection of priorities; however, the peer review system in place at the NIH continues to ensure that only the highest quality research is funded.

With regard to the issue of duplication, we believe that the very nature of scientific inquiry is a safeguard to unnecessary duplication of research. NIH-supported research is initiated by individual investigators with differing skills, interests, backgrounds and perceptions. Therefore each project represents a different approach to research questions. Research investigators and peer review members are quite knowledgable as to the past and current research being undertaken in their fields and are quick to identify unnecessary duplicative research. It is extremely unlikely that duplication of projects exists to a significant extent.

Although the biomedical sciences are inherently complex and are becoming more so with each new discovery, the NIH has long recognized the need for "streamlining" wherever possible. Fiscal constraint has made it all the more necessary to make the best and most efficient possible use of available resources. A good example of this approach is the NIH shared instrumentation program.

Question: Can you identify specific areas of duplication or overlap within NIH that could be combined or consolidated for the sake of economy?

Answer: We do not believe that duplication of effort in any research areas supported by the NIH occurs to any measurable degree. Although several Institutes may pursue research in similar areas (e.g., diabetes), the categorical nature of the Institutes precludes duplication. With a continuing decline in the award rate for research project grants from year to year, the program staff of the Institutes are acutely aware of all areas being supported. Unnecessary duplication is scrupulously avoided.

Question: What is the status of a proposed merger of NIH and NIMH?

Answer: No merger between NIH and NIMH is currently proposed. However, in April 1981, Senator Daniel Inouye introduced S. 925, a bill to transfer the National Institute of Mental Health to the National Institutes of Health. There has as yet been no action on the bill, which was referred to the Committee on Labor and Human Resources.

Question: Is such a merger feasible and would it result in significant savings of funds?

Answer: In response to an inquiry from Senator Inouye, before he introduced his bill, the NIH Director pointed out that, while many of the research and research training programs of the NIMH are consistent with the mission of NIH, NIMH clinical training functions and service programs are not. Furthermore, a transfer of the NIMH administrative structure would require a reorganization of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) -- a reorganization that would be initiated and conducted by the Secretary and the Assistant Secretary for Health.

As a result of the passage of block grant legislation, which removed many of the service functions from ADAMHA, an internal restructuring of that agency is underway. The Administration has no plans for further reorganization that would involve transfer of any of the ADAMHA institutes to NIH.

AUDIT REVIEW

Question: Your Division of Management Survey and Review makes audits at the request of NIH management. Why is this function under the Office of the Director, rather than the HHS Inspector General? To what extent is the location of the audit function at odds with the intent of the IG legislation--that is, to create a centralized, independent audit and investigation function within major departments?

Answer: The functions of the Division of Management Survey and Review (DMSR) are located in the Office of the Director, NIH, rather than the HHS Office of the Inspector General (OIG) because they do not fall within the OIG's purview. DMSR does not perform audits. All audits within HHS are performed by the OIG Audit Agency (AA). DMSR does, however, provide advice and assistance to NIH administrators on management control systems and safeguards for the use of Government funds, including contract and grant funds. Also, as a specialized and flexible resource to NIH management, DMSR performs a variety of special assignments and troubleshooting functions. Further, DMSR is the central NIH liaison point for relationships on matters involving the U.S. General Accounting Office (GAO), the Audit Agency on internal audit matters, and the HHS OIG Office of Investigations (OI) on investigative matters other than those involving internal security. In addition, DMSR has been designated to review and report on all cases received through the OIG hotline that are referred to NIH for action. In fact, handling such cases now constitutes a significant part of DMSR's workload.

Originally, because the NIH Director was concerned about a lack of internal review capability, DMSR was established to carry out a comprehensive audit program on NIH operations and activities. While DMSR was established in 1963 as the Management Audit Branch (MAB), it evolved over the next few years into an organization that could not accurately be characterized as an internal audit group. Rather, it had become a troubleshooting organization. Therefore, when all DHEW audit functions, both internal and external, were reorganized into a central DHEW Audit Agency, the decision was made at all levels that MAB should remain at NIH. Also, MAB was then assigned the liaison responsibilities for NIH with the Audit Agency on internal audit matters. To avoid any inference that MAB might still have audit responsibilities, the name of the Branch was changed to the Management Survey and Review Branch. Ultimately, it was changed to DMSR.

In a DHEW report leading to the centralization of all Department audit functions, the statement is made that "Audit does not replace management's responsibilities, at all levels, for self-appraisal. Centralized auditing in HEW should not affect management's responsibilities and abilities to appraise its own performance and make changes where appropriate." In fact, DMSR provides NIH management with the resource needed to exercise that responsibility.

As DMSR evolved from an internal audit organization into a troubleshooting organization, it also branched into the external affairs of NIH. In fact, about half of DMSR's recent assignments have involved visiting contractors' or grantees' sites. Those visits have primarily been made to review allegations about irregularities or abuses involving NIH programs, including scientific misconduct such as the fabrication of research results. While most of DMSR's assignments in the last several years have not been closely related to auditing, a few have been. In those cases, there has sometimes been a fine line of distinction between classifying the job as either an audit or troubleshooting assignment. However, the distinction has been made with reasonable accuracy. DMSR's assignments have concentrated on only certain designated facets of a contractor's or grantee's activities, as opposed to making a comprehensive audit of the contractor's or grantee's entire operations.

DMSR has a close working relationship with the OIG. It provides the OIG with a monthly listing of all its on-going assignments and routinely provides the OIG a copy of all its final reports. Also, when audit implications develop on any of its jobs, it informs appropriate officials of the Audit Agency on a timely basis. Further, if DMSR develops information indicating that fraud or any other potentially prosecutable offense might be involved on one of its jobs, it reports the matter to appropriate OI officials for their consideration. During the first 8 months of 1981, DMSR reported 18 such cases to OI officials. Conversely, when they have become aware of matters affecting NIH that are not within their purview, both AA and OI officials have referred these matters to DMSR for handling.

While allegations on irregularities or abuses involving NIH programs have sometimes been directed to DMSR itself, most have been referred to DMSR by others. Mostly, they have been referred by NIH officials who have received such allegations or who have become aware of possible irregularities or abuses through their normal duties. Also, as mentioned previously, some allegations have been referred to DMSR by AA or OI officials. Further, other organizations -- such as the HHS Office of the General Counsel, the GAO, and even members of Congress -- have referred such allegations to DMSR. Such matters have been referred to DMSR when the referring office has judged it appropriate that the matter be resolved by NIH.

Question: We understand that your audit division frequently reviews a single grant or contract involving only a minimal amount of funds. What can you tell us about this?

Answer: DMSR assignments are performed on a priority basis, with the circumstances involved in each case determining the priority placement. The significance of the matters involved, including the amount of the funds in question, if misuse of funds is involved, is taken into account when setting such priorities. To protect the integrity of NIH programs to the greatest extent possible, DMSR reviews all significant matters brought to its attention, staff resources permitting. When feasible, DMSR combines short-term travel to several organizations to better utilize its staff and travel resources.

Question: To what extent is the objectivity of your audit division compromised by being located in the very agency that makes the grants and contracts in the first place?

Answer: Since DMSR is located in the Office of Administration, Office of the Director, NIH, it is independent from the NIH components that actually award contracts or grants. Further, NIH administrators are very conscious that good management is crucial to carrying out their activities, and they are alert to the fact that program misuse and fraud can and does occasionally occur within NIH programs. This is evidenced by the prompt actions such officials have taken on the findings, conclusions, and recommendations DMSR has presented to them on the results of its various assignments.

INDIRECT COSTS

Question: We have been concerned about the award research grantees receive for indirect costs. Our figures show that indirect costs have increased from 22.6 percent of total NIH costs in fiscal year 1971 to 28.6 percent in fiscal year 1980. Where do we stand on these costs in the current fiscal year and what are the projections for fiscal year 1983? Give us the figures in absolute dollars and as a percentage of total costs.

Answer: The figures are, of course, incomplete for 1982. As of January 31, 1982, NIH had authorized nearly $377 million for total costs, of which approximately $112 million, or 29.7%, was for indirect costs. The final amount for 1981 was $655 million, or 29.5% of total costs. Looking ahead, we project an annual increase ranging from 0.5 to 0.8% based on historical trends.

Question: What is the impact on the amount made available for research grants -- is it shrinking because of the rising level of indirect costs?

Answer: Proportionately, funds available for direct costs have decreased progressively as a percentage of the total amount available for research grants while indirect costs have steadily increased. This pattern has continued uninterrupted since 1966.

Question: To what extent is a grant for indirect costs open-ended to permit a grantee to recover whatever he claims?

Answer: With a few exceptions, it has been the policy of DHHS (and its predecessor DHEW) since 1966 to provide for the full reimbursement of indirect costs. For NIH, this is accomplished through a final settlement procedure that allows for an adjustment to achieve an actual allowance (plus or minus) based on the application of a final indirect cost rate to the actual base expenditures. In this sense, the indirect cost allowance initially authorized is open-ended until time of settlement when the final reimbursement may be adjusted; in the majority of cases, no adjustment is necessary. While an adjustment could be either upward or downward, in the majority of cases increased funds are provided.

Question: Is this procedure followed by any other government agency making similar awards -- or is NIH unique in this respect?

Answer: We believe that the policy of reimbursing full indirect costs on the basis of final rates and actual expenditures is unique to the Department of Health and Human Services.

PERCENTAGE OF APPROVED GRANTS

Question: Is is correct to say that about 75% of approved grants will not be funded under the NIH FY 1983 budget? And if so, isn't it likely that researchers will leave the field of research to practice medicine as MDs or do research in other areas?

Answer: It is true that a large number of approved grants will not be funded, but it is also true that the grants with the highest promise of making scientific advances in areas of importance to the NIH missions will be funded at levels which will permit steady productivity. Some individuals will, indeed, be discouraged and turn to other means of serving the biomedical and health enterprise. Others will seek smaller amounts of money from their own institutions or private and community agencies to permit pilot and feasibility studies whose results will better their future chances of receiving NIH funding.

MISMANAGEMENT AND DATA FALSIFICATION

Question: Problems associated with the monitoring of research projects were the subject of Senate Committee on Labor and Human Resources hearings in 1981. A case involving data falsification by an NCI-supported researcher was the focus. Has the problem of misuse of funds by an NCI-supported researcher been resolved? What specifically has been done to redress this problem? What further steps will be taken?

Answer: The case discussed in the hearings before the Labor and Human Resources Committee is a very complex one involving matters of concern to both NIH and FDA. The fact-finding phase of the NIH investigation has been completed, and NIH investigators are completing their report and seeking corroboration from other sources. In response to a request from the researcher involved, NIH and FDA are examining ways to coordinate their actions in a combined proceeding. Any combined or separate proceeding will include an opportunity for the researcher to comment on the agencies' findings and present arguments in his own behalf.

Should FDA determine that violations of requirements for use of investigational drugs occurred, they would disqualify the individual; he then would be ineligible to receive or use investigational drugs. NIH sanctions could include a requirement for consideration of the agency's findings in review of subsequent applications for funding, prior NIH approval before certain research activities might be undertaken with NIH funds, or, if determined by the Secretary, debarment from eligibility for funding for some specified period of time.

Because of the issues raised by the Senate hearings and the NIH and FDA investigations, NCI conducted a thorough review of a grant subsequently awarded to this investigator at another institution, now in the second of three years of support. The Institute found that the researcher had failed to obtain review and approval from his institutional review board for a protocol involving studies with tissues from human cancer patients, and on those grounds suspended funding for studies involving human tissues. NCI also determined that progress on the portion of the grant involving laboratory animals was poor. Taking these shortcomings into account, along with the still unresolved issues attendant to the earlier funding of the investigator, the NCI elected to withhold the third year of support.

Question: How widespread is the problem of extramural fund mismanagement?

Answer: During the past few years there has been a significant increase in reports of misconduct involving NIH awards. Six of sixteen cases investigated during the past three years involve falsification of data. The others involve procedural or fiscal violations. To a great extent, this probably reflects an increased sensitivity and willingness to report real or apparent misconduct. The numbers are small viewed against the total numbers of awards, however. The dozen or so active cases represent only a tiny fraction of some 20,000 awards.

While misconduct in science hardly represents a problem of epidemic proportions, it is a matter of great concern to NIH. All research is aimed at discovering the truth, and the scientific method includes many safeguards against error and falsification. NIH is currently extending and refining its policies and procedures for dealing with incidents of real or apparent misconduct. The object is to ensure prudent stewardship of public funds while according equitable treatment to individuals whose conduct has been called into question.

Question: It has been suggested that decreasing the lengths of grants ensures greater accountability. Would you comment on the issue of shortening the length of NIH grants?

Answer: NIH generally favors long-term (3-5 years) periods of recommended support for biomedical research in order to enhance the stability and continuity of investigators' efforts. Scientific accountability is achieved through normal peer review assessment (both initially and through recompetition) as well as through annual review by program staff of both progress reports and non-competing application for continued support. This process may selectively be supplemented by project site or staff visits.

It should also be noted that the initial review process for grant applications requires a considerable expenditure in terms of NIH staff time and of costs associated with the consultants who comprise the review groups. If grants were to be shortened to 2-year periods, for example, the costs of the peer review process would essentially double.

Additionally, the NIH is very much aware of the time and expense involved on the part of potential grantees and grantee institutions in preparing applications. Indeed, in response to the concern grantees have expressed regarding this situation, the NIH has implemented several measures to reduce the paper work, and thus the time, associated with grant applications. It would be counterproductive to shorten the length of grants and thus increase expenses to the grantee institutions in preparing more frequent applications.

In summary, we do not believe that shortening the length of grant support would improve appreciably upon what is already a high degree of scientific and fiscal accountability.

BIOMEDICAL RESEARCH TRAINING

Question: This and previous Administrations have attempted to drastically reduce or entirely eliminate Federal funding for biomedical research training. NIH has reported over the past few years that training programs are already seriously deficient in providing new talent to the biomedical research community. What is your comment on this? In an era of Federal funding cutbacks, do you feel that NIH research training programs are once again in serious jeopardy?

Answer: While the total number of individuals in research training programs has been slowly reduced over the past five years, there is still support for approximately 9,000 persons in the system in 1983. Judicious selection of training sites and disciplines should prevent serious deficiencies in providing well trained investigators to advance the future of biomedical science. The core of the system should be able to withstand this modest entrenchment without appreciable diminution in the quality of the research training experience.

CENTERS/INTRAMURAL RESEARCH

Question: After being reduced slightly in fiscal 1982, the number of comprehensive and specialized centers grants is to rise in fiscal 1983--and funding is to increase by some 6%, or $15.9 million. What is the reason for this growth?

Answer: Research centers stimulate the cross-fertilization of ideas between scientists of various disciplines and thereby promote new approaches to the prevention, diagnosis, and treatment of disease. They also provide an important outlet through which new knowledge about prevention, treatment, diagnosis, and rehabilitation is transferred to community physicians. The proposed increase in funding for comprehensive and specialized research centers reflects an effort to maintain program balance among each of the NIH activities that span the biomedical spectrum from basic research to technology transfer.

Approximately $3 million of the $16 million increase will restore or initiate support for seven additional research centers. These centers will provide the means to meet exceptional research needs and opportunities. NCI will initiate support to centers that will foster the evolution of new knowledge of cancer, and will accelerate the transfer of knowledge of cancer, prevention, treatment, and care to health professionals and the general public. NIADDK will restore or initiate funding to research centers of great importance to research in the fields of cystic fibrosis, digestive diseases, kidney diseases, and diabetes. NIA plans to support a teaching nursing home that will allow researchers to have early contact with many health problems of aging that are often now seen only in acute, nonrehabilitative stages.

The remaining $13 million of the $16 million in additional funds represents a 5.2 percent increase over the 1982 level. This additional support to research centers will provide a measure of relief against the rising costs of doing research.

Question: Why do you propose a $32 million increase in intramural research when the number of new research grants is to be reduced?

Answer: Most of the additional funds proposed for the intramural program are necessary to cover the costs of administrative mandatory increases -- such as annualization of pay raise costs, within-grade salary increases, Federal Telecommunication System increases, and utility rate increases -- and to offset the effects of inflation on basic laboratory supplies and equipment as well as hospital supplies necessary to maintain ongoing basic and clinical research.

Another portion of the increased funding will be used for equipment and supply purchases that were deferred in 1982 and that are necessary to prevent serious erosion in the many areas of NIH research that depend on sophisticated biomedical technology. The increased funding will permit utilization of the new Ambulatory Care Research Facility at the Clinical Center in Bethesda and the National Institute of Environmental Health Sciences facility in North Carolina.

An increase for the intramural program is proposed in order to enable this program to maintain its vitality within the overall NIH research effort.

CAPPING INDIRECT COSTS

Question: We note you are planning to cap indirect costs associated with research grants at 90 percent. To what extent have you determined what the effect of this cutback will be on the colleges and universities involved? Since it may not be possible to identify each and every item under the label indirect cost, how can you be sure your cutback won't have some unintended effects which would impair research?

Answer: This matter has been discussed extensively with outside groups, particularly the Director's Advisory Committee. We cannot be certain at this time what the precise impact will be. In our estimation, however, essentially four things could happen:

- Certain institutional services to scientists may be curtailed or eliminated. We speculate that any such services would not be of an essential nature and that progress would not be seriously impeded.

- Efficiencies within the institutions may increase; therefore, they would be able to provide critical research facilities and services at lower costs than previously.

- It is possible that institutions may be able to find other sources of funding for indirect costs, which would have the added benefit of providing potential availability of support for direct research.

- Some institutions may, through reassessment, transfer some costs from the indirect to the direct category. Such procedures may ultimately result in less diverse accounting systems than is now the case.

I would like to emphasize that we view this as a temporary measure to allow time for consideration of approaches that may be available for long term policy.

RESEARCH PROJECTS

Question: The new budget proposes to fund 4,100 new and competing research project grants -- a reduction of 14 percent from the 1982 level of 4,741. If you reduce the amount of awards, won't that also reduce the productivity of a project?

Answer: Reducing the budget of an award may be met by an investigator in a number of ways: decreasing the number of personnel employed on a project, reducing the number of experiments done over a given period of time in an effort to conserve on supplies, and eliminating the personal presentation of data at meetings and the scientific interchange at conferences. The productivity of work should not be seriously affected, although it may take longer to produce the same results and disseminate the information.

Question: When was the last time NIH funded only 4,100 new research grants?

Answer: In 1977 the NIH funded 3,840 new and competing research project grants.

Question: What will this do to the forward progress of research that has been fostered at NIH in recent years?

Answer: It can be anticipated that research will continue to progress steadily forward but at a somewhat slower pace.

Question: To what extent are you reducing awards for new and continuation grants in fiscal 1983? By 4%? By 7%?

Answer: The direct cost reductions of approximately 3 to 4 percent applied to research grants in 1982 will be continued in 1983. There will be no reductions in direct costs for new and competing research grants in 1983.

Question: How did you arrive at the 4,100 grants? To what extent is the figure tied to the number of approved grants you expect to get from the peer review system?

Answer: In formulating the 1983 budget for NIH, we endeavored to fund as many competing research project grants as possible while maintaining the necessary balanced distribution of resources between research project grants and the other research and research training mechanisms. This distribution resulted in a total of 4,100 new and competing research project grants that could be funded. This figure is not tied to the number of grants approved for funding.

RESEARCH MODERNIZATION ACT

Question: Have you made an assessment of how the proposed Research Modernization Act (H.R. 556), if enacted, would affect the overall NIH budget and research efforts? Can you provide a dollar figure on how much money would have to be reallocated as required by this bill in its present form?

Answer: The Research Modernization Act (H.R. 556) would establish within the NIH a National Center for Alternative Research, with representation from each Federal agency that conducts or supports research and testing involving live animals. The Center would be charged with identifying and developing alternative research and testing methods, directing all Federal agencies to utilize such methods, evaluating the use of such methods, and educating scientists and the public as to the existence and use of such methods.

In lieu of providing new funds, H.R. 566 would require that 30 to 50 percent of the funds appropriated to each agency for research and testing programs involving live animals be redirected to the development of alternative methods. A preliminary analysis indicates that some $350 to $600 million in research dollars would be earmarked for reallocation if the legislation were enacted. This reprogramming would result in the termination of support for a large number of important research programs and would impede scientific progress in many areas of biomedical research.

Furthermore, it is unlikely that such a large sum could be as wisely expended by an entity concerned with developing alternative research methods as under our current system wherein various agencies support the development of non-animal technologies to assist them in solving specific research and testing problems.

Question: What's the Administration's position on this measure?

Answer: As expressed in a bill report signed by Secretary Schweiker in October 1981, the Administration opposes enactment of the Research Modernization Act, considering the legislation to be unnecessary and to detract seriously from the effectiveness and balance of DHHS programs.

NATIONAL TOXICOLOGY PROGRAM (NTP)

Question: The National Toxicology Program (NTP) is now 3 years old. It was initiated in order to coordinate efforts to identify chemicals in the environment of greatest risk to public health. What is the status of the National Toxicology Program (NTP) and how well -- or badly -- is it doing?

Answer: We have moved rapidly to fulfill our mission of improving the Federal Government's toxicological capabilities. I would like to cite a few examples of what I believe are significant achievements in this area.

First, we are moving rapidly toward an improved long-term bioassay, one which does not merely provide a simple yes or no answer to whether a chemical is carcinogenic, but which provides a more complete toxicological profile, including information on a wide variety of toxic endpoints other than cancer. In 1980, 40 percent of our bioassays incorporated special studies. This year, all our bioassays incorporate some special studies such as genetic toxicology, examination of effects on the kidneys, lungs, liver, the immune and reproductive systems, or those which affect neurobehavioral functioning.

Second, we are devoting an increasing percentage of our resources to developing good short-term tests, which will allow us to detect these kinds of health effects faster and less expensively. In order to become adequate substitutes for conventional toxicological testing, short-term methods must be sufficiently sensitive, minimize the detection of both false positives and false negatives, and be standardized so that when different laboratories use them they will produce identical results.

Finally, as the program has progressed, we have improved the mechanism by which chemicals are nominated and selected for testing for various toxic effects. These nominations come from a variety of sources, not only governmental but from industry, labor organizations, and academia as well. The nominations are evaluated by our staff and by our Board of Scientific Counselors. They are then published in the Federal Register for public comment. All this information is carefully evaluated before these chemicals are ranked as to their priorities for testing by the NTP Executive Committee which is made up of the regulatory and research agencies.

We have not been able to move as quickly as might be desired on two problems worthy of our attention; namely, the problem of assessing the toxicity of mixtures--the kinds of exposures people face in the world every day--and in developing improved methods for predicting on the basis of animal tests what the actual risk may be to humans. These are complex scientific issues. The speed at which they are resolved is more a function of how rapidly we gain new insights than of economic resources available.

The Program has been reviewed thoroughly on two occasions: by the Department's Office of the Assistant Secretary for Management and Budget in 1980 and by the Investigations and Oversight Subcommittee of the House Science and Technology Committee last year. In both cases, the Program was determined to be making good progress toward its goals.

Question: What is the status of the Program in NCI and NIEHS?

Answer: Dr. David P. Rall, the Director of NIEHS, also directs the National Toxicology Program to which the National Cancer Institute contributes. NCI is one of the nine members of the NTP Executive Committee. This committee provides policy guidance regarding the direction of program resources and priorities and plays a key role in the selection of chemicals to be tested. Historically, the NCI Bioassay Testing Program was part of NCI's Division of Cancer Cause and Prevention. When the NTP was formed in 1978, this program became a part of NTP. In July 1981, Secretary Schweiker approved the reorganization that shifted the Bioassay Testing Program to NIEHS to consolidate the major NIH components of NTP. Since the July 1981 decision, the NTP Deputy Director, Dr. John A. Moore, has managed the NCI portion of NTP directly as part of the NIEHS Toxicology Research and Testing Program.

This year NCI will make available $47.9 million to NIEHS for this effort. In 1983, the funds to support this effort are included in the NIEHS request.

Question: What is the status of coordination with other agencies?

Answer: The NTP is successfully improving the coordination of toxicological efforts both inside and outside the Department. The NTP research components--NIEHS; the National Center for Toxicological Research (NCTR), part of the Food and Drug Administration; and the National Institute of Occupational Safety and Health (NIOSH), part of the Centers for Disease Control--coordinate their activities closely through the NTP Steering Committee. Second, representatives from all of the nine agencies which participate in the NTP sit on its Executive Committee and are involved in selecting chemicals for testing, establishing testing priorities, helping develop protocols which are appropriate to the needs of both researchers and regulators, and developing policy guidance. The Executive Committee's regulatory agencies--the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), the Food and Drug Administration (FDA), and the Consumer Product Safety Commission (CPSC)--benefit from the timely exchange of information on the results of testing and methods development programs.

An example of this cooperation is NTP's special testing initiative on Benzidine and Benzidine Congener dyes. This effort to look at the toxicology of over a dozen dyes for mutagenicity, carcinogenicity and chemical disposition involves the Consumer Product Safety Commission, EPA, NCI, NCTR, NIEHS, NIOSH, and OSHA.

RECEPTOR SITES

Question: You seem to be developing a greater understanding of the role of "receptor site" defects in causing disease. Please bring us up to date on your progress.

Answer: It is known that the cell membranes that enclose each cell in our bodies contain protein "receptors," which selectively react with specific chemicals (or drugs) outside the cell--these receptors must fit the chemicals as precisely as a key in a lock--and then send appropriate signals to the interior of the cell, determining what action the cell should take. To function properly, these receptors must be able to make extremely fine chemical distinctions at every phase of the cell's life, beginning with the fertilization process. Sperm cells, for example, normally only recognize egg cells that belong to the same or to closely related species.

The failure of protein receptors to do their job properly may lead to a variety of diseases; new knowledge is being rapidly accumulated on this subject. Examples include the following:

- It has been shown that when receptors for low density lipoproteins are either missing entirely or are present in only low concentrations in the outer cell membrane, there is an accumulation of cholesterol in the blood stream (called hypercholesterolemia) and an accumulation of cholesterol in arterial walls (called atherosclerosis). Investigations initiated by grantees of the National Institute of General Medical Sciences, and now being continued by the National Heart, Lung, and Blood Institute, have delineated the basic details of this overall process. Steps are currently being taken to purify the receptors in the laboratory to identify their exact biochemical structure.

- Calcium has been shown to be essential for heart muscle contraction, and it has been learned that certain receptors on the surface of heart muscle cells are critical to this process. Knowing how this works, researchers have been able to develop calcium-blocking agents, such as the drug "verapamil," to control the rate of entry of calcium into the cell by blocking its receptors. This has become an important tool in the treatment of heart attacks.

- It has been discovered that, in non-muscle cells, a protein called calmodulin avidly binds calcium to keep it at a very low concentration until a signal is given for its release. This information is particularly important for understanding such fundamental processes as cell division and cell motility (movement).

- It has been learned that diabetes mellitus can exist not just because of a deficiency of insulin, but also in the absence of a sufficient number of receptors on the cell membrane to receive this hormone and produce the necessary response.

- The discovery of opiate receptors has led to the discovery of endorphins (endogenous morphines) and to investigations of their role in the control of pain.

- Dr. Henry Bourne, an NIGMS grantee from the University of California, San Francisco, has associated a hereditary disorder (pseudohypoparathyroidism, type I) with a deficiency of a cell membrane protein which, while not part of a receptor itself, has been found to be necessary for carrying the message to the interior of the cell that the receptor is occupied.

Question: To what extent are you suggesting that if we learn how to repair damaged receptor sites we can control various diseases?

Answer: The control of disease through intervention at the level of the receptor, is still a relatively new area. The repair of damaged receptors requires a precise knowledge of the nature of the receptor, and research to accomplish this is still in its infancy. In the meantime, however, efforts are being made to make up for the deficiency in the receptor by pharmacologic and genetic intervention. Examples of attempts to control disease by pharmacologic means include: the recently developed calcium channel blocking drugs, like verapamil, for treatment of irregular heart beats; the use of β-adrenergic receptor blocking drugs like propranolol to prevent recurrent heart attacks; and the use of the adrenergic receptor blocking drugs to treat asthma, which has been shown in many cases to be due to an increased number of receptors.

Question: What about endorphins--the body's own pain killers? How close are we to making better use of these?

Answer: There continues to be great scientific excitement over recent findings that simple peptides, such as the endorphins--opiates which are found in the brain--may act as central neurotransmitters. The discovery of these substances was prompted by basic studies of nerve cell receptors in the brains of experimental animals. Now we know that these substances come from the breakdown of much larger molecules, and that at least three classes of opiate receptors exist, each with distinct properties. Recent studies have also more precisely elucidated the mechanisms by which endorphins influence how nerve cells communicate with each other.

Research has substantially advanced our understanding of the natural functions of the endorphins, and continues to bring us close to the successful clinical application of this knowledge, not only for the alleviation of pain, but also possibly in such diverse situations as in shock where blood pressure falls to dangerously low levels, or in dementia where learning and memory skills fade, or in central nervous system injury where it is desirable to stimulate nerve cell sprouting and regeneration.

INDIRECT COSTS

Question: The National Institutes of Health has announced that indirect cost recovery on research grants will be reduced by 10%. Universities and medical schools will be the principal institutions affected. It is not contrary to practice to reduce federal costs by reducing indirect cost reimbursement? What effect will this have on the institutions?

Answer: The NIH has done more than any other Federal agency over the years to help grantee institutions gain appropriate reimbursement for the indirect costs of research. For example, the NIH has operated a unique after-the-fact settlement system based on final rates and actual expenditures; this system produced higher and more timely reimbursement than those that would result if the NIH had followed the practices of most other agencies. However, recognizing that the recent deceleration in the growth of research funding requires increased efforts to contain expenditures in every way possible, it seems imperative that we arrest the disproportionately rapid growth of indirect costs which has been underway for the last 15 years. Currently, indirect costs account for 30 percent of the total funds awarded through research grants; in 1966 the comparable number was 15 percent. The Department of Health and Human Services and awardee institutions must jointly seek means to contain indirect costs in the long-term. The proposed 10 percent reduction is intended as a temporary measure.

The expected effect of the proposed 10 percent reduction is discussed in the answer to the next question.

Question: Representatives of grantee institutions maintain that a reduction of indirect cost reimbursement will weaken institutional capacity to conduct research. Are they correct?

Answer: We cannot be certain at this time what the impact on the grantee institutions and their researchers may be. In discussions emanating from the numerous considerations on this matter within the NIH Director's Advisory Committee, the speculation has been that the impact may be felt in four ways: 1) certain institutional services to scientists may be curtailed or eliminated; 2) institutions may, in fact, become more efficient in the provision of services and facilities; 3) institutions may be able to locate other funding sources; and 4) some institutions may transfer some costs from the indirect to the direct category. We do not feel that any of these effects will markedly weaken institutional capacity to conduct research.

Question: When direct costs are cut back, the government and the institutions expect to reduce the scope of work to be done. What is NIH doing to permit an analogous reduction in scope in response to its reduction of indirect costs reimbursement? Will there be a corresponding cutback in federal regulations? Which regulations will you eliminate?

Answer: For the past 2 years, the NIH Director's Advisory Committee, a chartered body that advises the NIH Director on policy matters pertinent to NIH mission responsibilities, has engaged in intensive examination of ways in which to "de-regulate" the grants process. These initiatives are well underway, and we anticipate a continuing activity aimed at improving and simplifying the process wherever feasible. Of immediate impact, it should be noted that a reduction in the indirect cost allowance will guarantee that grantee cost-sharing requirements are satisfied and could eliminate the attendant paperwork associated with the cost-sharing proposal and documentation process.

Question: Did you consider other ways of cutting costs besides reducing indirect cost recovery? What were they? Why was indirect cost reimbursement the best course, overall?

Answer: NIH has absorbed reductions in all phases of its operations. It already has reduced direct costs provided in individual grants as well as made major reductions in its research contracts and intramural activities. Indirect costs cannot realistically be immune from sharing the fiscal burden. Moreover, direct costs further undergo the scrutiny of peer review where deletions and reductions are frequently recommended. This means that direct dollars are subject to a critical judgment which indirect costs are not; again, it is our belief that one element of cost -- namely indirect costs -- should not be impervious to necessary reductions.

Question: In dollar amounts, how much money will a major medical school lose because of this reduction in indirect cost reimbursement? Can you give some examples?

Answer: There is no way the NIH can predict this with certainty, even if one assumes that the awardee institutions will be unable to effect any economies or find other sources of support. However, we are preparing an analysis of the approximate impact on the top 20 NIH grantees and will share this with the Subcommittee shortly.

Question: Indirect cost recovery by institutions of higher education are based on OMB Circular A-21. Does the Circular authorize unilateral decisions to reduce indirect cost reimbursement?

Answer: OMB Circular No. A-21 and other cost principles deal with the allowability and allocability of costs, but they do not require a Federal agency to reimburse recipients fully. The fact that cost-sharing is mandated by statute for many grant and assistance programs is but one example of the intent of the Congress to distinguish a grant-in-aid from a procurement. There are other instances where either no indirect costs are provided or an indirect cost ceiling is imposed (e.g., foreign grants, conference grants, National Research Service Awards).

Question: In his letter transmitting Circular A-21 to federal agencies in February of 1979 the OMB Director said: "Agencies are not expected to place additional restrictions on individual elements of cost." Is not the NIH reduction of indirect cost reimbursement contrary to that principle?

Answer: We think not. As stated above, the cost principles do not mandate full indirect cost reimbursement. Fiscal constraints oblige us to exert greater discipline on our entire operations. Our plan is to include rather than exempt indirect costs from the area of consideration.

Question: In its effort to support a specified number of grants, NIH apparently has decided to reduce indirect cost reimbursement. By maintaining quantity, in this case 4,100 grants, is not NIH undermining the principle of funding scientific projects solely on the basis of merit?

Answer: On the contrary, the 1983 budget request is based in part on a reaffirmation of the traditional NIH policy of funding grants primarily on the basis of scientific merit. The proposed reduction in indirect costs will enable the NIH to fund approximately 600 more high-quality new and competing renewal projects than otherwise would be the case.

AWARD RATES AND PAYLINES

Question: What are the competing research project grant award rates and paylines, by Institute, for fiscal year 1983?

Answer: Estimated paylines and award rates for competing research project grants in 1983 are as follows:

	Payline	Award Rate
Cancer	190	26%
Heart	180	25
Dental	190	33
Arthritis	180	27
Neurology	190	35
Allergy	160	20
General Medical Sciences	180	39
Child Health	170	21
Eye	190	35
Environmental Health	200	26
Aging	190	15

CLINICAL TRIALS

Question: This year's House version of the bill specifically provided funds for nine approved clinical trials, but those funds were not included in the continuing resolution. Have any of the Institutes had the resources to begin these clinical trials, and if so, are they funded at levels necessary to adequately support the trials? Does the fiscal year 1983 budget provide any funds for implementation or continuation of these clinical trials? If budgetary constraints are such that clinical trials are unable to be pursued, doesn't this substantially retard our ability to bring research accomplishments to the bedside, and turn the NIH into strictly a research, rather than a research and development, agency?

Answer: Efforts on two of the nine high-priority trials listed in the House report on the 1982 Appropriations Bill will be initiated in 1982 under the current budget. The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases will fund a pilot study for the trial entitled "Relationship Between Blood Glucose Control and Vascular Complications of Insulin-Dependent Diabetes Mellitus." The National Heart, Lung, and Blood Institute and the National Institute on Aging will jointly fund a feasibility study for the trial entitled "Isolated Systolic Hypertension in the Elderly."

Three of the trials will be initiated in 1983, but at reduced levels. These are: "Efficacy Trial of a Combined H. Influenza-Peutussis Vaccine in High-Risk Populations" and "Anti-Viral Preparations Other Than Interferon," both supported by the National Institute of Allergy and Infectious Diseases; and "Spinal Cord Injury--Use of Drugs to Minimize Damage," supported by the National Institute of Neurological and Communicative Disorders and Stroke.

Several of the Institutes are initiating or continuing other clinical trials not listed in the House report. Thus, the NIH will continue to transfer research results to clinical practice as expeditiously as possible.

NIEHS CONSTRUCTION FUNDS

Question: With regard to construction funds for facilities at the National Institute of Environmental Health Sciences, were funds appropriated to other Institutes reprogrammed to cover such construction costs? If so, how much was reprogrammed from each Institute, and how was the reprogramming accomplished?

Answer: No funds were reprogrammed from other NIH Institutes to cover construction costs related to the NIEHS facility. In 1981, reprogramming authority for $2,425,000 was approved by the Senate and House Appropriations Subcommittees for uses related to construction of the National Institute for Environmental Health Sciences (NIEHS) research facility in North Carolina. In this action, $1,675,000 was reprogrammed from other projects within the NIH Buildings and Facilities account, and $750,000 was reprogrammed within the NIEHS intramural program.

RESEARCH GRANT REDUCTIONS

Question: Your budget justification makes reference to continuation of a 3 to 4 percent reduction in average cost for noncompeting continuation grants. Is any similar across-the-board arbitrary reduction contemplated or assumed for new and competing research project grants, and if so, reductions of what magnitide?

Answer: Average cost reductions of approximately 3 to 4 percent that were implemented in 1982 for noncompeting continuation grants will be continued in 1983. These reductions are not to be across-the-board arbitrary reductions and do not apply to any specific award. A similar 1982 reduction for new and competing grants will not be continued in 1983. However, all research grants will be subject to the 10 percent across-the-board reduction in indirect cost reimbursement. NIH will award 90 percent of the actual indirect costs based on the formally negotiated rates at each grantee institution.

INDIRECT COST CONTAINMENT

Question: We are aware you have an Advisory Committee looking into the issue of indirect cost containment -- and our Committee has requested a report on the matter. What are the results of these activities?

Answer: The NIH Director's Advisory Committee concluded that it would not be appropriate to arbitrarily limit indirect costs as a single category of expense. In light of current fiscal constraints, however, the NIH believes that a concerted effort to contain indirect costs is needed and, as a step toward that end, proposes to reduce reimbursements in 1983 by 10%. The NIH report on containment of indirect costs in research was recently submitted to your Committee on Appropriations. I would like to insert a copy for the record.

REPORT ON CONTAINMENT OF INDIRECT COSTS IN RESEARCH

INTRODUCTION

In its report on the fiscal year 1982 budget request for the Department of Health and Human Services, the Committee on Appropriations stated:

> "The Committee notes that the Director of NIH has appointed an Advisory Committee to look into methods for dealing with indirect costs. The Committee encourages these efforts and directs the Department to report by next February on the measures it has taken or plans to take for containing the growth of indirect costs." (Senate Report No. 97-268, p.49)

The following report has been prepared by the National Institutes of Health of the Department of Health and Human Services in response to this instruction.

BACKGROUND

Since 1966, indirect costs have increased progressively both in terms of actual dollars and as a percentage of the total amount awarded. For FY 1981, indirect costs for NIH grants amounted to 29.5 percent of total costs. The steady increase in indirect costs has been a source of considerable concern because it has significantly reduced the funds available for direct research costs.

Historically many myths and misunderstandings have surrounded indirect costs. Some perceive these costs as a "profit" to the recipient institution and associate high numerical rates with inefficiency. Many argue that indirect costs reduce the availability of the "real" costs of research, by which they mean direct costs. In fact, indirect costs are not a profit and an indirect cost rate in and of itself has little meaning. No logical conclusion can be drawn simply by comparing rates among institutions nor can one determine the reasonableness of indirect cost reimbursement on the basis of the rate alone. Moreover, indirect costs are, indeed, real costs. The classification of particular expenditures as direct or indirect costs depends in part on the institution's organization for managing its business affairs and its methods of managing research. The two classes of expenditures are equally necessary for an institution to conduct its activities and each type is as true a cost as the other.

Direct costs are generally understood because they are clearly identifiable and related to specific projects whereas indirect costs are not readily identifiable with a particular project or activity, but nevertheless are necessary to the general operation of the institution. Examples of such costs are utilities, maintenance of grounds and facilities, depreciation, departmental administrative expenses, and library costs.

While recognizing the need for and importance of indirect costs, NIH and its advisors are nevertheless concerned about the rising costs of biomedical research. During the past year, as one part of this overall concern, the NIH Director's Advisory Committee, a chartered body that advises the NIH Director on policy matters pertinent to NIH mission responsibilities, engaged in an intensive effort to examine the many different types of expenditures, including indirect costs, that are associated with biomedical research. The objective was to identify appropriate ways to reduce or contain such costs wherever feasible.

The Committee recognized that indirect costs are both real and necessary and that their proper reimbursement is an essential requirement in preserving health research capacity. The Committee concluded that it would not be appropriate to impose a uniform or maximum indirect cost rate on all institutions receiving NIH research awards or to take other arbitrary steps related to this single category of expense. This consensus supports the basic position taken by the United States Comptroller General in a July 27, 1979 report wherein it was recommended that if Federal participation in health research costs is to be limited, the limit should be effected through some formal ceiling on Federal reimbursement of total costs.

Possible Steps to Limit Reimbursements for Indirect Costs

While NIH agrees in principle with the consensus position stated above, the prospect of curtailed funding, coupled with rising costs generally, have led us to consider some possible changes in the way indirect costs are reimbursed that merit further examination. For example, using the negotiated indirect cost rate applicable at the time of each award, NIH could set the allowance for indirect cost at that level and rescind the current practice which allows for settlement adjustments based on final rates (usually upward). This would be similar to the practice of the National Science Foundation, the Department of Defense, and virtually all other Federal agencies. If NIH were to adopt this approach, it collectively would reduce its grantees' claim for additional indirect costs by an estimated $10-15 million annually. Such a practice would result in many cases in a final aggregate recovery of indirect costs which is less than actual unless the grantees were able to effect offsetting economies in their operations.

Another step that could be taken would be to redefine the categories of eligible and ineligible expense with respect to reimbursement of indirect costs. For example, certain university administrative expenses could be defined as ineligible expenses, thus eliminating indirect cost recovery for these cost elements from grant and contract support. Conversely, amortization of the capital costs of research equipment, now an ineligible item, could be made eligible. Such a pattern of charges could be effected so that indirect costs were easier to understand and justify and that total Federal outlays were reduced. Again, grantees would receive less reimbursement for indirect costs and would have to eliminate some expenses or find other sources of funding.

The NIH is working closely with officials in the Office of the Secretary, DHHS, to determine whether either or both of these changes should be initiated through changes in DHHS grants policies and, if so, how and when they should be implemented. We will keep the Committee apprised of the progress in this area. In either case, the impact of limiting indirect cost recovery needs to be carefully weighed as it relates to the progress and success of the research activity overall.

It should be noted that the FY 1983 budget request provides for a 10 percent reduction of reimbursements for indirect costs. NIH plans to implement the proposed budget reduction through an arithmetical application in the centralized Indirect Cost Management System, thus limiting the allowance to 90 percent of actual indirect costs based on each formally negotiated rate. This would accomplish a proportional across-the-board reduction for each grant that now receives full indirect cost reimbursement; similar reductions would not be imposed on those select programs (e.g., Institutional National Research Service Awards) that already are limited in the overhead they may recover (e.g., 8 percent of total allowable direct costs). Reimbursing indirect costs at the "90 percent of eligible" level should be an efficient and uncomplicated way to achieve budget economies in the immediate future and allow time for consideration of alternative approaches, such as those described above, that may be more suitable as a basis for long term policy.

QUESTIONS SUBMITTED BY SENATOR PROXMIRE

REDUCTION IN INDIRECT COSTS

Question: How much money will be saved in fiscal year 1983 as a result of limiting indirect costs on NIH research awards to 90% of the negotiated rate?

Answer: Approximately $70 million would be saved in 1983 as a result of limiting reimbursement for indirect costs on research grants to 90% of the negotiated rate.

Question: How many additional new grants will be funded in fiscal year 1983 as a result of this policy?

Answer: The policy of reducing indirect costs on grants will permit the NIH to fund approximately 600 additional new and competing research project grants in 1983.

Question: What specific reductions would NIH make if Congress disapproved the new policy but without adding additional funds to the budget request?

Answer: If Congress disapproves the policy on indirect cost reductions but does not provide additional funds, the NIH would necessarily fund fewer new and competing research project grants. However, we would review all our programs to assess the possibility of absorbing part of the reduction in other mechanisms.

Question: If the NIH received an additional unrestricted $70 million from the Congress, how much would be used, if any, to restore the reduction in indirect costs?

Answer: If the NIH received an additional unrestricted $70 million from the Congress for 1983, the funds would not be used to restore the reduction in indirect costs. Our first priority would be to fund additional new and competing research project grants. In this category, an additional $70 million would permit the award of about 600 more new and competing grants, for a total of 4,700.

Question: Are there any exceptions of the 10% reduction policy?

Answer: The reduction will be imposed only on those grants which customarily receive full indirect cost reimbursements. Reductions would not be imposed on grants that are already limited to the indirect costs they may recover such as research training and research career programs.

Question: Some have argued that the quality of research will be significantly impaired as a result of this policy. What is your view?

Answer: Although it is too early to predict the precise effect, the NIH is confident that the type and quality of research will continue in essentially its present form. The peer review system assures that only the best research is funded.

Question: What is your best judgment as to how grantee institutions will adjust to the 10% reduction in indirect costs?

Answer: This matter has been discussed extensively with outside groups, particularly the Director's Advisory Committee. In our estimation, essentially four things could happen:

- Certain institutional services to scientists may be curtailed or eliminated. We speculate that any such services would not be of an essential nature and that progress would not be seriously impeded.

- Efficiencies within the institutions may increase; therefore, they would be able to provide critical research facilities and services at lower costs than previously.

- It is possible that institutions may be able to find other sources of funding for indirect costs, which would have the added benefit of providing potential availability of support for direct research.

- Some institutions may, through reassessment, transfer some costs from the indirect to the direct category. Such an effort would achieve more stringent evaluation of these individual items of cost and could ultimately result in less diverse accounting systems than is now the case.

Question: Is there any reason to believe that the 10% reduction may cause some grantees to review their own administrative and overhead expenses more closely and eliminate expenditures that are less essential?

Answer: As mentioned in response to the preceding question, we believe that the 10% reduction may result in the curtailment or elimination of certain institutional services to scientists. We do not anticipate that any such services would be of an essential nature; thus the research effort would not be seriously impaired.

Question: Do you consider the 10% reduction to be a permanent policy or as a transition to a new permanent policy on indirect costs?

Answer: The indirect cost proposal was developed in the context of our attempt to maximize the number of new and competing research project grants that could be supported within an austere budget, and at the same time maintain a proper balance among the research activities NIH supports. The proposed 10% reduction is viewed as an efficient and uncomplicated way to achieve budget economies in the immediate future and allow time for consideration of approaches that may be more suitable for long-term policy.

Question: What are some of the future options you are considering for arresting the increase in indirect costs?

Answer: The prospect of curtailed funding, coupled with rising costs generally, has led us to consider several possible changes in the way indirect costs are reimbursed that merit further examination. For example, using the negotiated indirect cost rate applicable at the time of each award, NIH could set the allowance for indirect cost at that level and rescind the current practice which allows for settlement adjustments based on final rates (usually upward). This would be similar to the practice of the National Science Foundation, the Department of Defense, and virtually all other Federal agencies. If NIH were to adopt this approach, it collectively would reduce its grantees' claim for additional indirect costs by an estimated $10-15 million annually. Such a practice would result in many cases in a final aggregate recovery of indirect costs which is less than actual unless the grantees were able to effect offsetting economies in their operations.

Another step that could be taken would be to redefine the categories of eligible and ineligible expense with respect to reimbursement of indirect costs. For example, certain university administrative expenses could be defined as ineligible expenses, thus eliminating indirect cost recovery for these cost elements from grant and contract support. Conversely, amortization of the capital costs of research equipment, now an ineligible item, could be made eligible. Such a pattern of charges could be effected so that indirect costs were easier to understand and justify and that total Federal outlays were reduced. Again, grantees would receive less reimburesment for indirect costs and would have to eliminate some expenses or find other sources of funding.

The NIH is working closely with officials in the Office of the Secretary, DHHS, to determine whether either or both of these should be initiated through changes in DHHS grants policies, and, if so, how and when they should be implemented. In either case, the impact of limiting indirect costs recovery needs to be carefully weighed as it relates to the progress and success of the research activity overall.

Question: What have been the trends in indirect costs as a percentage of total research costs since 1966?

Answer: In 1966, indirect costs accounted for approximately 15% of the total funds awarded through research grants and have risen steadily in each subsequent year to the current level of nearly 30% total funds awarded.

Question: How much was expended for indirect costs in fiscal year 1981 and how much is estimated to be spent in fiscal year 1982 and 1983?

Answer: The amount for indirect costs in 1981 was $655 million. In 1982, we estimate that indirect costs will be $672 million. The estimated amount for 1983, assuming the 10% reduction policy is adopted, is $630 million.

NATIONAL CANCER INSTITUTE

STATEMENT OF DR. VINCENT T. DeVITA, DIRECTOR

ACCOMPANIED BY:

DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. JANE HENNEY, DEPUTY DIRECTOR

PHILIP D. AMORUSO, EXECUTIVE OFFICER

JOHN P. HARTINGER, FINANCIAL MANAGER

NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. Our next witness for this afternoon is Dr. Vincent DeVita, Director of the National Cancer Institute.

Doctor, it's a pleasure to see you again, and we appreciate your being with us. If you'd introduce your colleages, and briefly summarize your statement, we will go on with the questioning.

INTRODUCTION OF ASSOCIATES

Dr. DEVITA. Thank you, Mr. Chairman.

On my immediate left is Mr. Hartinger, who is the Budget Officer for the Cancer Institute. Sitting behind me on my left is Dr. Jane Henney, the newly appointed Deputy Director of the Cancer Institute, and Mr. Philip Amoruso, who is the Associate Director for Administrative Management. Of course, you have met the other gentlemen at the table.

Mr. Chairman, I will submit my full testimony for the record, and since Dr. Malone has already mentioned some of our management initiatives, I'd like to submit for the record two booklets that describe these initiatives in more detail rather than cover them in my brief comments.

[CLERK'S NOTE.—The material was submitted and has been placed in the subcommittees files.]

Also, this is the 10th anniversary of the national cancer program, and the National Cancer Advisory Board has prepared a document which I believe was sent to Members of Congress already.

PREPARED STATEMENT

Senator SCHMITT. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. VINCENT T. DEVITA

I am pleased to be here to discuss our progress in cancer research and new management initiatives that improve the program's efficiency.

We just observed the tenth anniversary of the National Cancer Program, and I can report that the progress since 1971 is significant. The first five-year survival data gathered from our Surveillance, Epidemiology and End Results (SEER) program show a relative survival rate of 45 percent for all patients diagnosed with cancer from 1973 to 1979. The relative rate is an estimate of the probability of escaping death due to the diagnosed cancer, if all other causes of death are not operating. Except for cancers of the breast and prostate gland, the relative survival rate is a reliable indicator of improvements in the management and curability of cancer in general in the United States. As a contrast, an earlier study--conducted before SEER was established--showed that patients diagnosed between 1967 and 1973 had a relative survival rate of 40 percent.

In human terms, Mr. Chairman, such a five percent difference, which is actually a 12.5 percent increase, means that an additional 320,000 patients diagnosed in the 1970's are potentially curable. These gains are a heartening measure of the progress we have made over the past decade. They reflect the individual advances made in cancer treatment and the reductions in age and disease-specific mortality nationwide that we have reported to this Committee in the past few years.

Recent major management improvements at NCI will contribute to future progress by husbanding our resources for the most promising research programs. Our management actions include:

- A centralized budget formulation and corporate decision-making process: All business management functions are consolidated in the Office of the Director. An NCI executive committee with broad scientific expertise assures that our resources are spent as effectively as possible across divisions.

- Major corrective changes in NCI's contracting process itself: All contracts now receive a more extensive, uniform review by non-government experts. A concept review before a contract is initiated assures that only high priority programs get precious resources and that old programs are phased out at appropriate times. Merit review of submitted proposals was improved. Administration of contracts is tightly controlled now and monitoring is close. These and many other changes are detailed in two publications I would like to submit for the record: The National Cancer Institute Contracting Process and Peer Review of Contract Proposals at the National Cancer Institute.

(Clerk's note: A copy of the reports, "The National Cancer Institute Contracting Process," and "Peer Review of Contract Proposals at the National Cancer Institute," are in the subcommittee's files.)

- An analysis of each of the Institute's 1150 contracts during 1980: Such a look was necessary because priorities and opportunities in cancer research had changed since 1971 when many of our large contract programs were established. This analysis helped identify $40 million of activities that could be reduced or eliminated in

Fiscal Years 1980 and 1981. We redistributed some of the savings to new programs and others to increase support of investigator-initiated research in our research project pool.

- Reorganization of the large contract that operates the Frederick Cancer Research Facility: We are recompeting the Frederick contract as five contracts instead of one, we reduced funding for the basic research component by 29 percent, and we appointed an NCI manager for the facility. We also moved several of our intramural laboratories to Frederick. This move allowed us to decompress facilities on the NIH campus and to consolidate others that had been temporarily housed in rented space.

As a result of these management initiatives, Mr. Chairman, we have been able to support the most important ongoing programs, begin new programs to capture research opportunities, and eliminate unproductive and marginally productive activities.

I would like now to highlight promising new areas of activity. As you know, the thrusts of the NCI's program in cancer research are: (1) cause and prevention, (2) detection and diagnosis, (3) treatment, rehabilitation, and continuing care, and (4) basic biology. I will present our program, its changes and promising new directions in terms of NCI's four operating divisions. Each incorporates one or more of these thrusts.

The Institute's recently organized Division of Resources, Centers and Community Activities is mounting two new programs which have our highest priority. One is expected to have major impact on cancer prevention; the other will upgrade the level of cancer care in communities all over America.

The first new program takes advantage of the fact that certain chemicals can prevent cancer. In fact, many of these chemopreventive agents are found in our diet--vitamins A, C, and E, selenium and certain chemicals called antioxidants. Research of the 1970's has shown that these substances can prevent the formation of cancer in animals exposed to cancer-causing agents. And epidemiologic studies of human populations in the United States and England suggest that persons who eat foods high in vitamin A or its precursor, betacarotene, have fewer cancers of certain kinds, such as lung cancer, even though those individuals were at high risk, because of heavy smoking, for example.

We now are testing the chemopreventive properties of retinoids (vitamin A-related compounds) in two populations at especially high risk of cancer: women with early precancerous cell changes in the uterine cervix (cervical dysplasia) who often develop uterine cancer; African albinos, almost all of whom develop skin cancer from exposure to sunlight.

We are collaborating with the National Heart, Lung, and Blood Institute to determine whether beta-carotene, a dietary precursor of vitamin A, is effective in protecting normal individuals from getting cancer. Although it will be given in pill form, beta-carotene is present in carrots, deep yellow and green leafy vegetables and yellow-hued fruit. The Heart Institute is using the same population to determine whether aspirin can protect against heart disease. We plan to support additional chemoprevention studies this year.

The Division's second new program, aimed at improving cancer care, takes advantage of the fact that more than 85 percent of cancer patients receive their primary care in community hospitals. Despite the availability of promising experimental treatments in specialized cancer centers, patients are often unable or unwilling to leave their homes, families and local physicians to obtain that special care.

Last June, we began working with community physicians to establish links between community hospitals, cancer centers and the large cooperative groups conducting our clinical treatment research. Within the next year we hope to establish 100 to 200 community clinical oncology programs (CCOPs) geographically located so that they can conveniently serve most Americans. These community programs will provide the link between community health care and the leading edge of cancer treatment research. We believe these programs will not only provide the most modern therapy to cancer patients, but will accelerate the modification and improvement of cancer treatment modalities and hasten the decline in national mortality from cancer.

In the Division of Cancer Treatment, research continues on biological response modifiers--substances that boost, direct or restore the body's natural defenses against cancer. We have nearly completed early (Phase I) clinical studies of three of these substances--natural interferon, thymosin and MVE-2. In Phase I trials of human interferon produced by genetic engineering, NCI scientists determined the therapeutic dose and the side effects. The compound for this study was supplied to us at no cost by Hoffmann-La Roche Inc.

Over the past year, we took additional steps to reduce costs and to streamline the development of anticancer drugs. One way in which savings were effected was by eliminating our plant collection program. This step was possible because a large number of plant products now are sent to us for testing from a variety of sources and at no cost. We will use the savings from this and other program changes to establish new centers for drug synthesis and testing and to expand the monitoring of early clinical trials--an activity critical in assuring the safe use of investigational drugs.

We are proposing a new radiation research program that would consolidate all our extramural research in this field including that on low-level radiation. radiation therapy, and diagnostic imaging. This latter area includes the research grants in diagnostic radiologic research transferred to us from the National Institute of General Medical Sciences last year. The new program will give a structure not only to our current radiation-related research, but also to any foreseeable responsibilities delegated to us.

Last year NCI scientists isolated and characterized the first virus associated with a human cancer. This work at NCI was confirmed when a similar, if not identical, virus was isolated again in Japan, where the particular form of leukemia associated with the virus is endemic. This is a landmark discovery. Now that we understand the cause of this form of cancer, we can work toward preventing it.

The activities of the Division of Cancer Cause and Prevention were reorganized during the past year. We transferred the carcinogenesis testing program, which examines chemicals for their ability to cause cancer in animals, to the National Toxicology Program headquarters in Research Triangle Park, North Carolina. That program is now staffed entirely by the National Institute of Environmental Health

Sciences, although NCI continues to serve on the Executive Committee and to participate in the selection of chemicals for testing.

The Division's new emphasis is on finding test tube or other alternatives to animals for testing agents suspected of causing cancer and is shifting its research goals in applied prevention to find ways to interfere with the promotion stage of cancer causation, as mentioned in my discussion of prevention using vitamins and other constituents of our diet. Our most important investment remains in research to understand the molecular events that initiate and promote cancer, and in exploring leads that link laboratory findings with cancer among human populations.

An important event occurred in the field of chemical carcinogenesis. Using recombinant DNA technology, NCI-supported scientists captured the genes that may be responsible for causing chemically transformed cells to grow uncontrollably like cancer cells. The exciting part about this finding is that those genes contain a switch similar to that carried by RNA tumor viruses. Such a switch can turn on normal cellular genes causing them to produce too much of a product at the wrong time in the life of a cell.

A related finding suggesting that gene changes may be at the very core of the cancer process was made by NCI investigators. They provided the first molecular evidence that a chemical carcinogen induces a very specific change in the DNA of an important gene in human cells. The product of this gene determines the shape of a cell, how it moves and what it adheres to.

The Division of Cancer Biology and Diagnosis supports research in tumor immunology. This field of cancer research has changed more than any other over the past ten years. What we knew about tumor immunology in 1971 was just the tip of the iceberg. And our nonspecific approaches to immunotherapy have for the most part been unsuccessful because the tools we used were crude, nonspecific stimulants of the immune system. With genetic engineering techniques and pure (monoclonal) antibodies produced with hybridoma technology, we have gleaned new insight into the role played by cells of the immune system in fighting cancer, and how those cells are turned on or suppressed. We now have monoclonal antibodies to several forms of human cancer, including the most common forms--breast, colon and lung. Scientists are testing the specificity of these preparations. In the future, such antibodies may be attached to radioisotopes for diagnosis or to anticancer drugs or radioactive compounds for targeting treatment.

Mr. Chairman, the request for the National Cancer Institute for Fiscal Year 1983 totals $955,449,000. This is an increase of $12,420,000 over the 1982 estimate.

This concludes my statement. I am prepared to answer questions and to supply additional information for the record.

BIOGRAPHICAL SKETCH

Name: Vincent T. DeVita, Jr., M.D.

Date & Place of Birth: March 7, 1935; Bronx, New York

Education: 1957 - B.S. (Chemistry) College of William and Mary, Williamsburg, Virginia

1961 - M.D. (With distinction) George Washington University School of Medicine, Washington, D.C.

Positions Held:

1961-62: Internship, University of Michigan Medical Center, Ann Arbor, Michigan

1962-63: Residency in Medicine, George Washington University Medical Service, District of Columbia General Hospital, Washington, D.C.

1963-65: Clinical Associate, Laboratory of Chemical Pharmacology, National Cancer Institute, Bethesda, Maryland

1965-66: Senior Residency in Medicine, Yale-New Haven Medical Center, New Haven, Connecticut

1966-68: Senior Investigator, Solid Tumor Service, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

1968-71: Head, Solid Tumor Service, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

1971-74: Chief, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

1974-80: Director, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

1975- Clinical Director, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

1980- Director, National Cancer Institute, National Cancer Program, National Institutes of Health, Bethesda, Maryland

1981-85 Member, Awards Assembly, General Motors Cancer Research Foundation

Academic Appointments:

Associate Professor of Medicine, George Washington University School of Medicine, Washington, D. C., 1971-75
Professor of Medicine, George Washington University School of Medicine, Washington, D.C., 1975-

Editorial Boards:

Associate Editor, Journal of the National Cancer Institute, Bethesda, Maryland, 1968-74
Scientific Editor, Cancer Chemotherapy Reports, National Cancer Institute, 1970-74
Advisory Editor, Journal of Radiation Oncology, Biology, and Physics, 1975 -
Associate Editor, Editorial Advisory Board, Cancer Research, 1977-81
Member, Board of Medical/Scientific Consultants, Cancer Nursing, 1978-80
Member, Board of Scientific Council, "Cancer Chemotherapy and Pharmacology," 1977-
Associate Editor, Cancer Clinical Trials, 1977-
Member, Editorial Board, Amer. Federation of Clinical Oncologic Soc., 1977-78
Member, Editorial Board, American College of Physicians (A.C.P.)
Audio Cassette Program, 1979-1980
Member, Editorial Board, Seminars in Oncology, 1979-84
Associate Editor, The American Journal of Medicine, 1978-1981

Member, Editorial Advisory Board, Breast Cancer Research and Treatment, 1980-
Member, Editorial Board, Your Patient & Cancer, 1980-
Member, Editorial Board, Gynecologic Oncology, 1981-
Member, Editorial Board, Hematological Oncology, 1981-

Committees and Other Offices:

Councilman, Assembly of Scientists of the National Cancer Institute, National Institutes of Health, 1968-70
Chairman, Program Committee, American Society of Clinical Oncology, Inc., 1972
Clinical Research Committee, NCI
Board of Directors, American Society of Clinical Oncology, 1973-76
American College of Surgeons Commission on Cancer, Committee on Patient Care and Research, 1975-78
Advisory Committee on Clinical Investigations II - Chemotherapy and Hematology, American Cancer Society, Inc., 1975-76
Publications Committee, American Society of Hematology, 1975-
WHO Expert Advisory Panel member, 1976-
Board of Directors, American Association Cancer Research, 1976-79
Lasker Award Jury, 1976-
President, American Society of Clinical Oncology, 1977-78
Chairman, Treatment Committee of the French-American Agreement, 1976-
Chairman, Special Membership Committee, American Association for Cancer Research, 1978-79
Member, Panel of Consultants on Clinical Oncology, International Union Against Cancer, 1979-82
Member, Awards Assembly, General Motors Cancer Research Foundation, 1981-85

Specialty Board Certification:

Diplomate of the National Board of Medical Examiners, 1961
Diplomate of the American Board of Internal Medicine, 1968
Diplomate in the Subspecialty of Hematology, American Board of Internal Medicine, 1972
Diplomate in the Subspecialty of Medical Oncology, American Board of Internal Medicine, 1973
Recertification, American Board of Internal Medicine, 1974

Professional Societies:

Fellow, American College of Physicians
American Medical Association
American Society of Hematology
American Society of Clinical Oncology
American Association for Cancer Research
American Federation for Clinical Research
American Society for Clinical Investigation, elected May, 1972
Society of Surgical Oncology (Ewing Society), 1976-1979

Honors and Awards:

Alpha Omega Alpha Medical Honor Society
Smith-Reed-Russell Medical Honor Society
Tobacco Research Industry Fellowship, Mount Desert Island Biological Laboratory, Bar Harbor, Maine, 1959
Award by the Government of Peru, "Oren del Sol en el Grando de Official," 1970
Visiting Professor of Medicine, Stanford University School of Medicine, July, 1972
Albert and Mary Lasker Medical Research Award, November 16, 1972
First Annual Clowes Lecture, Roswell Park Memorial Institute, October, 1973
DHEW Superior Service Award, 1975
Esther Langer Award, June 1976
Alumni Medallion, College of William and Mary, October 1976
Jeffrey Gottlieb Award, November 1976
Karnofsky Prize, 1979
Griffuel Prize, Association for the Development of Research on Cancer, Paris, December 1980

Marital Status: Married, one child

Present Address: 9925 Julliard Drive
Bethesda, Maryland 20034

RESEARCH EFFORTS

Senator SCHMITT. I think it is appropriate to note that event in more than just passing—10 years in any kind of an effort is an important milestone. It is about the attention span of the average 16-hour-a-day, 7-day-a-week researcher. At least that's been my experience. And also it is usually the point where you have achieved some sort of level or plateau or peak in your efforts.

Do you feel that the Institute has in fact peaked in its initial efforts at research? Has it reached a plateau? Is it gathering itself for new endeavors and new heights? What is the current situation?

Dr. DEVITA. "Hitting our stride" is a better way of looking at it from my point of view. I have never seen greater opportunity for preventing the diseases we know as cancer. There is clear evidence there has been considerable progress in the past 10 years.

There are three areas I would like to touch on. The first relates to changes in survival rates over the past decade.

The second one relates to advances that have taken place in the past year that have revolutionized our thinking in terms of the biology of cancer.

And the third relates to the point you have just raised. I believe we have now reached critical mass in the national cancer program, a critical mass that allows us to do the things envisioned in 1971 when the Cancer Act was passed.

Senator SCHMITT. So the past is prolog.

Dr. DEVITA. Yes, indeed, sir.

CANCER INVESTIGATORS

Senator SCHMITT. Do you find it is roughly the same people out there doing the work now that started out in the first few years, or do you have a whole new generation coming on board?

Dr. DEVITA. We have trained a whole generation of scientists.

Senator SCHMITT. But are there jobs for them?

Dr. DEVITA. Yes, by and large they are gainfully employed in research. We increased the number of new grantees fourfold during the early years of the cancer program when the funds increased very rapidly, so we have really expanded the pool of investigative workers in cancer research over the past decade.

RECENT RESEARCH ADVANCES

The results, in my view, are astonishing. The biologic revolution is one way of describing it. I think in the past year alone we have found out that there are multiple genes, including some perfectly normal ones, that can cause cancer. Experiments called "transfection" where genes from human cancer cells are removed and put in mouse cells, have been shown to cause the mouse cells to become malignant. We can identify those genes. In many cases they appear to be organ specific, that is, there may be a cancer gene for every different type of cancer. This matches the clinical truth that there are over 100 different kinds of cancer.

We have also found that the genes we have known existed in viruses for many years that caused cancers are also normal counterparts of human chromosomes. What really causes cancer is how they are strategically inserted into the cells. So now we have a plethora of genes to work with that are cancer genes.

The technology that Dr. Malone referred to, the DNA recombinant work and monoclonal antibodies, are the main tools to analyze these genes.

In the past few months we have isolated the gene for interferon gamma, which has been quite elusive over the past couple of years. We have discovered probably the first real human tumor virus. This is a very interesting story in itself. And we are now using monoclonal antibodies in clinical studies either by themselves as diagnostic tools, or for treatment after they are loaded with "warheads," such as poisons and radioisotopes.

All these things are products of research supported by the NIH. Not even considering the human benefit, that is, the improved survival rate that we see now, these advances represent most significant progress.

STRIDES DURING PREVIOUS 10 YEARS

Senator SCHMITT. Where were you 10 years ago?

Dr. DEVITA. NCI started the SEER program, surveillance, epidemiology, and end results, in 1973 with new cancer program funds. SEER provides us a way of monitoring cancer incidence and survival. We now have 5-year relative survival rates, from 1973 to 1979; they are 45 percent for all races combined. We have a comparable figure for 1967 to 1973 but not a comparable data base; that figure is 40 percent. So we have seen about a 12.5-percent increase—a 5-percent difference—which I think reflects all those advances in treatment for specific cancers we have described to the committee in the past.

The other point I can make is that we are now taking the information we have on cancer prevention and shifting from the testing of chemicals for cancer-causing properties, which is now done by NIEHS, to devoting NCI's attention to prevention by trying to understand the mechanisms of, and interfere with, the late stages of carcinogenesis. We are setting up a series of programs in our cancer control program that should allow us to set national goals in defined populations for both reducing the incidence of cancer by these prospective trials and also decreasing the mortality.

That is why I say in the 1980's we are just "hitting our stride." This required some managerial changes which are described in my submitted testimony.

The budget that we are defending for fiscal year 1983 is $955,449,000; I'd be pleased to continue on this line of questioning.

Senator SCHMITT. Please, sir, go ahead with your testimony.

Dr. DEVITA. I think I just finished it. [Laughter.]

Senator SCHMITT. I thought you might have. At least you have given it before.

PRION PARTICLE

Did I read recently of the discovery of a new form of organism that is capable of incorporating genetic material from the host body that might have some cancer implications?

Dr. Malone, you are sitting there nodding your head.

Dr. DEVITA. I'm not sure you're talking about——

Senator SCHMITT. I'm not sure what I'm talking about. I just glanced at an article the other day.

Dr. MALONE. I believe that Senator Schmitt is referring to the newly discovered prion particle.

Dr. DEVITA. Yes; this was actually mentioned earlier in the record. This is primarily a new type of protein agent. We have not had as yet any information about it with reference to cancer.

INDIRECT COSTS

Senator SCHMITT. Relative to your Institute, do you have anything to add to the impact of the cap on indirect costs for research grants at 90 percent of actual cost?

Dr. DEVITA. No; I believe it's been adequately covered, especially in terms of not allowing that portion of the research grant funds to grow beyond what we provide directly to investigators.

We are, of course, using the money recouped from the 10-percent reduction in indirect costs to pay for more new grants.

IMPACT OF BUDGET REDUCTIONS

Senator SCHMITT. Anything special on the impact of the reductions of last year on the Cancer Institute that might not have been covered by Dr. Malone?

Dr. DEVITA. We took a bigger percentage of the reduction from our contract program, and we accelerated some changes that we would have made perhaps over a year longer. One was to change the early stages of our drug development program to reduce our plant collections. Another step was to close down a facility we were intending to close but doing it a year sooner. We also took a 4-percent reduction from our grantees which in effect had the same effect as described by Dr. Malone.

Senator SCHMITT. Is there any research path that you were planning to follow that you are not going to follow until this budget crisis is over?

Dr. DEVITA. No, sir; I am pleased to say we are in the process of rolling over some programs that have served their purpose simultaneously with the creation of some of the new ones I mentioned. It's a little bit tricky to phaseout programs and start at the same time. This is the reason why we changed the entire management profile of the Cancer Institute, which is unique in its size and structure on the NIH campus.

Senator SCHMITT. I must go vote again. We'll recess for 10 minutes.

[A brief recess was taken.]

TRANSFER OF NATIONAL TOXICOLOGY PROGRAM

Senator SCHMITT. The hearing will come to order again.

We understand, Doctor, that the bioassay program for testing chemical compounds has been transferred to the Environmental Health Institute along with about $50 million.

Dr. DEVITA. Yes, sir.

Senator SCHMITT. Could you give me the rationale for this and your own opinions on it?

Dr. DEVITA. The Secretary approved the transfer this year, Mr. Chairman. We suggested it in early 1980, because we felt that, as Dr. Rall pointed out earlier this morning, testing the animals should include more than just the end-point cancer. Therefore, biomedical research would be better served if the program was in an institute that is looking for multiple toxic effects of the chemicals on kidney, brain, and so forth. If we were starting a new effort today, we'd put it where it is now. I fully supported the transfer.

Senator SCHMITT. Do you have a specific coordination mechanism in place to make sure that your Institute is fully aware of what is going on in the bioassay program?

Dr. DEVITA. Yes; first, as it was before, NCI and NIEHS jointly managed it and found that to be cumbersome. Single management is much better. NCI is represented on the executive committee of the national toxicology program which approves the bioassay program. We also have a chemical selection group within the Cancer Institute which makes nominations to the NTP for testing.

ANTICANCER DRUGS

Senator SCHMITT. Relative to the recent publicity on anticancer drugs and their potential toxicity, do you have any comments that you wish to make on that issue—for the record.

Dr. DEVITA. For the record, it was an unfortunate series, from my view, Mr. Chairman, because it was full of inaccuracies that frightened a number of patients away from cancer therapy. Toxicity was overemphasized. The negative was emphasized without any of the positive side. That's the biggest criticism of it. Approximately 46,000 patients a year in this country owe their lives to cancer drugs. That fact alone, if emphasized, would have provided some balance.

Senator SCHMITT. Have there been any significant anticancer drugs discovered since 1970?

Dr. DEVITA. Oh, yes, indeed. The drug development program, which in 1974 cost $46 million a year, is now running at about $40 million per year. If you consider the effect of inflation, we really cut it by about 50 percent, and yet it's turning out the same number of drugs per year as it did in 1974. We have some very exciting drugs.

As a matter of fact, most of the drugs that were heavily criticized in the Washington Post series will undoubtedly turn out to be useful when testing is complete.

Senator SCHMITT. So what would have been the situation now relative to the success in curing or mitigating the effects of cancer if we had not undertaken this specific effort to develop drugs useful in fighting cancer?

Dr. DeVita. The relative survival rate, as I quoted before, is from a 10-percent sample of the entire country. I have gone through the survival rates tumor by tumor and examined what I believe is the impact of drug therapy. In 1955 we had no drug therapy to cure any cancer; today we estimate, based on 1980 data, that about 46,000 patients a year are alive as a result of drugs used alone or in addition to surgery and radiotherapy.

This is a fairly significant impact for a short period of time.

And the future is ahead of us because there are 185,000 people a year in this country who are operated on for cancer, and although the surgeon removes all visible cancer, the tumor recurs—metastasizes. These patients are prime candidates for the addition of some other kind of therapy—drugs or biologicals, which may prevent recurrence.

NATURALLY OCCURRING ANTICANCER AGENTS

Senator Schmitt. Tell me: Is the certification of drugs that are merely concentrations of natural body chemicals easier than artificial chemicals that are not normally found in the human body?

Dr. DeVita. What we find when we use any material in pharmacologic rather than physiologic doses, it has side effects that it might not otherwise have had. You and I have interferon in our blood right now and are not feeling it. It's a very small amount. But if we gave you 200 million units of interferon, you would be fatigued and would have fever. So at pharmacologic doses it has side effects. Some of the cancer drugs are worse than that. Some are quite toxic, and can cause a great deal of trouble.

Senator Schmitt. You are including drugs that are in fact heavier concentrations of natural body chemicals?

Dr. DeVita. Yes, indeed.

Senator Schmitt. But how do they compare in their side effects? Is there any way you can make a comparison in their side effects to artificial chemicals?

Dr. DeVita. So far, the ones we are testing have less side effects. Of course, the efficacy, whether they work or not, is the key point. If a drug or a drug combination works and cures 50 percent of a certain kind of cancer, and the patient feels poorly for a period of several months, it's better than something that doesn't work but causes no side effects.

This is the perennial problem we have when we speak to patients about accepting therapies that are available today, if they have been promised something that works but has no known beneficial effects, like laetrile.

INTERFERON

Senator Schmitt. When do you expect the first useful results from the clinical trials using interferon to be available?

Dr. DeVita. Some of them are available right now, Mr. Chairman. The phase I studies have been completed.

Senator SCHMITT. This is the bacterially produced interferon?

Dr. DEVITA. Yes; when we first discussed this, 2 years ago, we were talking about the impure interferon made from cell cultures. Shortly after, a pure interferon became available, and we tested both. All I can say at this point is that the preliminary results confirm the earlier observations that interferon has some antitumor effect. We're still working on dose relationships and schedules and the like.

The interesting observation to me, at least, in looking at the results so far, is that the tumors that tend to respond are well differentiated, that is, they look most like the normal tissue. The tumors that are poorly differentiated respond better to the anticancer drugs that we now have, the synthetic chemicals, and so on. We can see the potential marriage of the use of both materials either in sequence or in combination.

Senator SCHMITT. Has there been any clinical measurement of the tendency for interferon to be produced as a function of different types of cancer?

Dr. DEVITA. I'm not quite sure what you mean—whether patients who have cancer produce interferon on their own?

Senator SCHMITT. Yes; the natural production of interferon. Has that been measured as a function of the type of cancer?

Dr. DEVITA. We know that cancer patients can produce interferon. The blood levels achieved naturally are nowhere near the levels that we are giving when we give the pharmacologic doses of interferon.

Senator SCHMITT. What I'm getting at is: Is that a way to determine what types of cancer would be most susceptible to interferon treatment?

Dr. DEVITA. I don't believe so, by measuring the level in the blood. However, there are assays we are using now growing cancer cells in soft agar that can detect responses to cancer drugs, and there have been some researchers in Arizona who have used interferon in this system, and in fact the results seem very similar. If you can control the growth in soft agar, the patient may respond.

PI-MESON TECHNOLOGY IN CANCER TREATMENT

Senator SCHMITT. Finally, Doctor, current plans are to terminate the cancer experiments utilizing the meson facility at the Los Alamos National Laboratory.

Dr. DEVITA. Yes.

Senator SCHMITT. Assuming that that termination goes forward, do you have any plans to make sure that what has been learned besides the application of mesons to cancer treatment can transfer into other areas of cancer research and treatment, such as the focusing of high energy on a specific model tumor?

Dr. DEVITA. Yes; I must say, Mr. Chairman, I was one of the great enthusiasts for pi-mesons, and we are all disappointed that the results haven't been better but pleased that the data were precise enough to give us some direction in terms of where to go with particle therapy.

Senator SCHMITT. What do you mean results have not been better?

Dr. DEVITA. The results of pi-meson therapy have not been significantly better than photon therapy in the machine configuration that exists at Los Alamos. When you examine the pure physics, we were talking about a monochromatic pi-meson beam, where you could deposit all the energy in a very small area around the tumor. It turns out that at the Los Alamos facility only about 10 percent of the energy of the beam is deposited at the Bragg Peak in the tumor. That means a lot of normal tissue, which we thought was going to be out of the radiation field, does receive low-energy radiation which puts it very close to photon radiotherapy.

There is one machine in Switzerland with a circular configuration that inputs the beam from 60 different points that may get around this.

Another problem with the facility is its access to patients because of its remote location.

Senator SCHMITT. Is it really the pi-mesons that are important, because it's not going to be your average hospital that can have a linear or even circular accelerator.

Dr. DEVITA. The circular one costs $25 million.

Senator SCHMITT. So shouldn't we be looking for what else we learned from those experiences, such as the CAT scan modeling of tumors?

Dr. DEVITA. In 1979, we embarked on an experiment in three different directions, the testing of neutrons in medically dedicated units as well as maintaining the pi-meson facility at Los Alamos, and a proton facility in Massachusetts. The third direction was to use drugs in conjunction with photon radiotherapy to sensitize tumors so that they are injured maximally while the normal tissue is not.

We have clinical studies with radiosensitizers and radioprotectors in conjunction with photon beams. Obviously, drugs plus ordinary X-ray equipment would be cheaper than use of particle therapy. So we are interested in examining the relative merits of each.

We have not closed the books on the pi-meson facility. We expect to see another grant application. We will continue the followup of the patients who have been treated at the facility until such time as there is no need for followup. And we will watch the Swiss facility with great interest to see if we should make further investment in pi-meson facilities of that type in the future based on what they have learned from the circular configuration.

SUBMITTED QUESTIONS

Senator SCHMITT. Thank you, Doctor. We will have some questions for the record, and we appreciate your time with us today.

Dr. DEVITA. Thank you, sir.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

BUDGET REDUCTIONS

Question: Have you discontinued any programs because of lack of funds?

Answer: We have not discontinued any programs because of lack of funds in fiscal year 1982 but the level of effort in many areas has been reduced.

Question: What impact have budget cuts had on your biomedical research programs?

Answer: Although no discrete programs have been eliminated, budget cuts experienced thus far in fiscal year 1982 have necessarily resulted in less-than-recommended support for recipients of National Cancer Institute grant awards. Reductions have also been taken in both the Institute's intramural research and research supported by contract. Research project grants -- both competing and noncompeting -- have been scaled down with an overall 4 percent reduction. However, the Institute has been able to increase the number of competing grants it is supporting by 38. Contracts supporting research in such areas as epidemiology, carcinogenesis, preclinical treatment and diagnostic research have also experienced slight reductions. In addition, several on-going research and research support programs have been targeted for more rapid reductions than originally anticipated. These activities include the screening and natural products portions of the drug development program, the Baltimore Cancer Research Program, related resource contracts, and various Cancer Control activities. Funds to support construction of safe and adequate biohazard containment facilities have also been diminished. The investigations which have been slowed in fiscal 1982 span all areas of research, i.e., cause and prevention; detection and diagnosis; treatment; and basic cellular research.

Question: What impact have they had on your training programs?

Answer: Under the National Research Service Awards Program, the number of full-time eqivalent trainees will be reduced from 1,531 trainees in 1981 to 1,305 trainees in 1982 and may impact on the future pool of highly-trained cancer researchers.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982 -- and how much will you spend in fiscal 1983?

Answer: The National Cancer Institute plans to spend $72,662,000 on cancer research centers in FY 1982. The FY 1983 budget request includes $75,024,000 for research centers.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: The present system of peer review examines the grant application for each grant, including core center grants, and recommends the deletion of specific aspects of the proposal that do not warrant federal support. This review process already imposes economies on the applicant. In addition, over the recent past, the National Cancer Institute has been funding the approved and eligible for funding core grants at less than the peer reviewed recommended level, i.e., last year's level plus a modest cost-of-living factor. This has allowed the National Cancer Institute to maintain a higher number of centers. We are continually looking to further economize and maximize our research investment in conjunction with the peer review system. Through the negotiation and administration of these grant awards, the Institute is better able to ascertain and justify the specific associated costs.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: In FY 1983, the National Cancer Institute can continue to effect economies that were started last year in the direct operations and program management areas primarily through consolidation of its business management functions. Many initiatives have been instituted which already have and will continue to reflect savings to the cancer program. While not included in direct operations, the increase in the cost of inhouse research by the Institute has been reduced by the closing of off-campus laboratories and the consolidation of research efforts either on the National Institutes of Health reservation or at the Frederick Cancer Research Facility. Reorganization of the large contract that operates the Frederick Cancer Research Facility is underway. The Frederick contract is being recompeted as five contracts instead of one, funding for the basic research component of the contract has been reduced by 29 percent, and a National Cancer Institute manager has been appointed for the facility. Also, several of the National Cancer Institute's intramural laboratories have been moved to Frederick. This move allowed decompression of facilities on the National Institutes of Health campus and consolidation of others that had been temporarily housed in rented space.

All of the resources available to the Institute, including space and positions, have undergone a careful scrutiny with a resultant reallocation of these resources within the Institute. This has also permitted the Institute to initiate several new laboratories by a redirection of these resources. Support to the Baltimore Cancer Research Program has been transferred from an intramural research component to a center grant (at a reduced level).

Question: What are your most important administrative concerns -- and what are your least important concerns?

Answer: Recent major management improvements at the National Cancer Institute will contribute to continued progress in achieving the most efficient use of National Cancer Institute resources for the most promising research programs. These high priority management initiatives include:

-- Increased emphasis on grant and contract monitoring, including the allocation of additional resources, with careful monitoring of all costs in this area, including travel and supplies;

-- A centralized budget formulation and corporate decision-making process with all business management functions consolidated in the Office of the Director. A National Cancer Institute Executive Committee with broad scientific expertise assures that our resources are spent as effectively as possible across the major National Cancer Institute divisions;

-- Major corrective changes in the National Cancer Institute's contracting process through which all contracts now receive a more extensive, uniform review by non-government experts. A concept review before a contract is initiated assures that only high priority programs get precious resources and that old programs are phased out at appropriate times. Merit review of submitted proposals has been improved. Administration of contracts is more tightly controlled and monitored; and

-- An analysis of each of the Institute's contracts was completed during 1980. Such a look was necessary because priorities and opportunities in cancer research had changed since 1971 when many of our large contract programs were established. This analysis helped identify $40 million of activities that could be reduced or eliminated in fiscal years 1980 and 1981. We redirected some of the savings to new programs and others to increase support of investigator-initiated research in our research project pool.

These management initiatives have allowed support of the most important ongoing programs, the beginning of new programs to capture research opportunities, and the elimination of unproductive and marginally productive activities. While all administrative concerns of the National Cancer Institute are important, these initiatives are currently considered to be of the utmost importance.

Question: What criteria do you use for determining your administrative priorities?

Answer: The National Cancer Institute has centralized its budget formulation activities within the Institute and created a corporate decision-making body to assure that administrative priorities and programs are reviewed. In addition, advice and guidance in setting National Cancer Institute priorities is sought through active participation of the National Cancer Advisory Board in the decision-making process. Also, each of the National Cancer Institute's major operating divisions receive input and guidance from their specific Boards of Scientific Counselors. Each division presents detailed information and budgetary data regarding all of their programs to these Boards which are composed of outside scientists, eminent and knowledgeable in the appropriate areas of scientific endeavor. Moreover, these Boards are now encouraged to communicate and interact with the overall National Cancer Advisory Board to assure more universal review of, and open communication about, all National Cancer Institute research programs and budgetary priorities.

LACK OF A DEPUTY DIRECTOR

Question: To what extent has the lack of a Deputy Director at the National Cancer Institute had adverse impact on the administration of the Institute?

Answer: I am pleased to notify you that Dr. Jane Henney was just approved for appointment as Deputy Director, National Cancer Institute. Dr. Henney is an expert clinician and has a wealth of government experience, having served in a number of key positions in the Institute. Her appointment is an important addition to the staff which will greatly enhance the scientific management and direction of the National Cancer Institute.

TOXICITY OF CANCER DRUGS

Question: You are, I know, well aware of the controversy created by the Washington Post series of articles on anti-cancer drugs. To what extent has the series proved valuable in focusing attention on any problems that may exist?

Answer: Unfortunately, the Washington Post reporters' attempt to focus on the real issue of the risks and benefits of anti-cancer drug therapy was distorted by the presentation of anecdotal cases which emphasized the toxic properties of anti-cancer drugs. In many cases, the reporters' interpretation of the medical facts of the case and potential uses of the drugs mentioned were incorrect.

Had the series presented a more balanced presentation of the choices that face the patient who has advanced cancer, and a more effective grappling of the issue of the benefit-risk of a toxic compound, a service to the public might have been accomplished.

Question: To what extent has it confirmed your fear that cancer victims might back away from using anti-cancer drugs?

Answer: During the initial weeks following the Washington Post stories, we received calls from many physicians across the country expressing concern that their patients would refuse further therapy. Fortunately, most cancer patients are thoughtful people who were not dissuaded by the imbalance of the articles and continued with their treatments. It is impossible to estimate the number of future patients who will be influenced by the reading of the articles and will pursue no therapy or alternative methods that are scientifically unproven.

Question: In a follow-up to the series, one of the authors stated that virtually all of the anti-cancer drugs were discovered "before 1970" and that virtually no better drugs have been found since. What is your comment on this?

Answer: Our experience has shown that an average of about ten years or more is required from the time of "discovery" to the establishment of efficacy and marketing of a useful drug. Methyl CCNU, Adriamycin, VP-16, Cis-platinum, Bleomycin and Hexamethylmelamine all were established as effective agents in the 1970's, although their actual discovery occurred earlier. Drugs discovered in the 1970's are still in various stages of evaluation.

We are now in the process of determining their efficacy and optimal role in the treatment of cancer. A number of these new drugs currently undergoing preclinical or clinical evaluation appear to show promise. Potentially effective new drugs include m-AMSA, DHAD, Indicine-N-Oxide, and Interferon. All have produced responses and are entering advanced stages of clinical trial.

The time frame mentioned above is similar throughout the pharmaceutical industry for nearly all drugs.

Question: What, if any, guidelines do you have for determining when to stop testing an anti-cancer drug because it either does not work or is too toxic for human use?

Answer: Every protocol involving experimental anti-cancer drugs contains explicit criteria stipulating the number of patients to be entered into that study. This is true for all phases of clinical investigations. Proper accrual of patients is monitored in two ways. Firstly, regular periodic reports of scientific progress submitted by investigators are reviewed with particular emphasis on the appropriateness of accrual. Secondly, supply of investigational drugs is linked to anticipated accrual. When a protocol is approved, the quantity required to complete the study is allocated to that study. Requests in excess of this amount require written explanation and National Cancer Institute review before approval.

Any clinical investigation involving experimental anti-cancer drugs may be discontinued at any time if it becomes evident that the toxicity of the agent is worse than the complications of the disease at that point. Cancellation of treatment may be initiated by the investigator or by the National Cancer Institute. As a result of the requirements to report serious side effects (adverse drug reactions) to the National Cancer Institute immediately, the National Cancer Institute has the capacity to discontinue an unsafe protocol at any time. Additionally, the National Cancer Institute Decision Network annually reviews the progress of each experimental drug. This committee is composed of twenty-five senior staff of the National Cancer Institute's Division of Cancer Treatment from the clinical and preclinical areas. Drugs which are judged by the Decision Network as ineffective or unsafe are discontinued from further testing in human subjects.

ANTI-CANCER DRUGS CONTROVERSY

Question: How well informed are the professional staff of cancer clinics about the toxic side effects of certain experimental anti-cancer drugs?

Answer: The National Cancer Institute has an extensive series of mechanisms in place which inform physician-investigators about toxic effects of experimental drugs. Before any physician may use an experimental anti-cancer drug, he must first write a protocol which describes the conditions of its use. This document, which is reviewed and approved by National Cancer Institute staff, contains a thorough description of all known toxic effects. The review process by the National Cancer Institute assures a comprehensive description of these effects. Another important source of information about experimental drugs is the clinical brochure. This document, prepared by National Cancer Institute staff, includes all clinically relevant information about the drug. It contains a section with a complete description of all known toxic effects. Clinical brochures are made available to all physicians utilizing the drug.

Another important channel of communication is the reporting of adverse drug reactions occurring during the course of ongoing studies. Physician-investigators, who are reminded annually of their responsibilities in this area, report adverse reactions promptly to the National Cancer Institute. Information about genuine adverse drug reactions are rapidly disseminated to the research community by the National Cancer Institute by mail and telephone.

Finally, toxic effects of anti-cancer drugs are a topic of intense scientific interest. They are frequently discussed at national and international meetings of cancer researchers.

Question: How well informed are patients receiving experimental anti-cancer drugs about their toxicity?

Answer: The essence of the process of informed consent is a full discussion between the doctor and his patient about the risks and benefits of any potential treatment. Neither the patient nor his doctor can make a reasoned judgment about any new treatment without a full consideration of its potential risks. Discussion of toxic side effects of anti-cancer drugs is, therefore, an essential part of both the verbal and the written basis of the informed consent process. The informed consent document for every protocol in which an experimental drug is to be used is reviewed by both the Institutional Review Board as well as the professional staff of the National Cancer Institute to ensure that it contains a complete description in lay terms of these potential adverse effects. Finally, since July 1981 new regulations of the Department of Health and Human Services concerning informed consent have required that the patient be given a copy of the consent form which he signs.

Question: What is the formal procedure for obtaining patient consent for the use of experimental anti-cancer drugs?

Answer: The procedure for obtaining informed consent from patients receiving anti-cancer drugs is no different from informed consent procedures for any experimental drug research. In essence, the physician obtains the consent from the patient to participate in a research protocol approved by an Institutional Review Board and the National Cancer Institute. The patient and the doctor sign a consent form which has been approved by both the National Cancer Institute and the local Institutional Review Board. A copy of this document is retained by the patient and the original is placed in his permanent medical record.

Question: To what extent should improvements be made in procedures for informing patients of the possible adverse consequences of receiving certain experimental anti-cancer drugs?

Answer: The essence of the consent process is to ensure that the patient is fully and adequately presented with benefits and risks of the proposed treatment. This is done in both written form and personal discussion. The informed consent document contains a complete discussion in lay terms of known or suspected adverse effects. This document is carefully reviewed by both the Institutional Review Board at the local hospital as well as the National Cancer Institute. A significant new change in the Department of Health and Human Services regulations requires that the patient retain a copy of this consent document. This permits the patient to review information about adverse effects at his or her discretion. These procedures provide an excellent basis for ensuring fully informed participation in research drug studies.

Question: Can you provide an example of the standardized patient consent form?

Answer: Although there is no single standardized patient consent form, all forms contain the following major elements:

- State that it is research, explain purposes, describe procedures and identify experimental procedures.
- Describe risks.
- Describe benefits.
- Describe alternatives.
- Describe confidentiality.
- Explain compensation/treatment for injury sustained as a result of protocol.
- Say whom to contact for answers in regard to research and subjects' rights.
- Say whom to contact in event of unforeseen injury sustained as a result of protocol.
- Explain rights to refuse and withdraw.

An example of a consent form follows:

NATIONAL INSTITUTES OF HEALTH

CONSENT FORM FOR MULTI-INSTITUTIONAL CONTROLLED TRIAL OF ADJUVANT CHEMOTHERAPY IN THE TREATMENT OF OSTEOSARCOMA, A PHASE III STUDY.

INFORMED CONSENT

PATIENT______________________________ DATE____________________

DIAGNOSIS: Osteosarcoma

You (your child) have osteosarcoma, a malignant (cancerous) tumor which arises in bone. The best treatment of this tumor has not yet been defined and a number of very important questions remain concerning the optimum treatment of this disease. You (your child) are being asked to participate in a clinical study designed to determine the role of chemotherapy in the treatment of this disease and to determine the best timing of chemotherapy.

Up until the early 1970's the prognosis for children with osteosarcoma was poor and less than 25% of children survived without developing recurrences of the tumor. Most of these recurrences were in the lungs. Radiation therapy and chemotherapeutic agents (drugs) which are effective in other pediatric tumors are not particularly effective in osteosarcoma. Nevertheless, physicians hoping to improve the prognosis for their patients treated children with osteosarcoma with the available drugs. Indeed, there seemed to be some beneficial effect in that as many as half of the children treated with chemotherapy after surgery did not develop recurrences. Initially, the improved prognosis for children with osteosarcoma was attributed to the drug therapy which was used. However, more recent studies have cast doubt on this point. In the past ten years there have been many medical advances, particularly in diagnosis of tumors and metastases with new x-ray techniques. Children with osteosarcoma may be diagnosed earlier today than in the past. All of these other factors seem to have contributed to the improved prognosis for children with osteosarcoma independent of the use of chemotherapy. As many as 40-50% of children with osteosarcoma diagnosed today and treated with surgery alone may survive without developing recurrence. If this is true then chemotherapy has contributed very little in the treatment of osteosarcoma. On the other hand, the actual contribution of chemotherapy to improved survival may be substantial. Unfortunately, there are many side effects of chemotherapy which will be outlined below, and some of the drugs will produce permanent side effects.

If you (your child) agrees to particpate in this study, you (your child) will be randomized between two possible treatment alternatives. The choice of treatment group will be made by a statistical process and there is an equal (random) chance of being appointed to either group. One group will receive chemotherapy which will begin approximately 2 weeks after surgery of the primary tumor and will last for almost one year. The drugs that will be used and their side effects are listed below. The other group will not receive chemotherapy immediately but will be observed very closely in the outpatient clinic. No further treatment will be given unless you(your child) develop recurrence of the tumor. If the tumor recurs surgery will be performed to remove the recurrent tumor and then chemotherapy will be given. The same chemotherapy will be given as outlined for the first group of children but only these children who develop recurrence of their tumor will be treated with chemotherapy.

Your physician believes that there is no way, at the present, to choose whether immediate treatment with chemotherapy after surgery or the delayed administration of chemotherapy for children who develop recurrence is the best treatment.

There are potential risks and benefits for patients assigned to either treatment group in this study. Patients who receive immediate chemotherapy, after surgical removal of the primary tumor, will all be subjected to the real and potential risks of the chemotherapeutic agents (see below). Your physicians feel that these toxicities are manageable but certain side effects are unavoidable. Every effort will be made to minimize these side effects. If immediate chemotherapy after surgery is the best form of treatment for this tumor, then the group randomized to receive immediate chemotherapy after surgery will have the benefit of the best treatment.

Patients randomized to the treatment group receiving no immediate chemotherapy have potential benefit of avoiding all of the toxic side effects of chemotherapy. Only the children who develop recurrence of their disease, and thus who presumably demonstrate a need for chemotherapy, will be subjected to the side effects of chemotherapy after they have relapsed. On the other hand, patients randomized to the delayed chemotherapy treatment group have the potential risk that recurrent tumor may be more difficult to treat successfully because of the number and size of the recurrent tumors. If chemotherapy does have a beneficial effect in the treatment of osteosarcoma, the chemotherapy may be most useful before the tumor has recurred and maybe less effective for children who have developed recurrences of their tumor.

Although the two treatment options appear to be very different, it is unknown at this time which treatment will be superior. Should it become clear during the course of this study that one of the treatments is superior to the other all children will be given the more effective treatment.

Chemotherapy. The drugs that will be used for patients who are to receive chemotherapy are listed below, along with possible side effects associated with each. Because these drugs will be given together we anticipate that there will be more side effects. Doses will be adjusted in order to minimize these side effects without diminishing the effectiveness of the drugs.

1. Methotrexate. This is administered intravenously over four hours. Its side effects include nausea, vomiting, depression in the blood counts, kidney damage, mouth ulcers and diarrhea. The antidote to methotrexate is leucovorin which is administered orally 24 hours after the methotrexate begins. Prior to each course of methotrexate treatment, a special evaluation of kidney function will be obtained. If the results are not satisfactory, treatment will be omitted or delayed.

2. Adriamycin. This drug is administered intravenously and if it escapes from the vein it may cause burning and destruction of the skin. Anticipated side effects include nausea and vomiting, ulceration in the mouth, diarrhea, blood count depression, loss of hair and liver abnormalities. One important side effect of adriamycin is damage to the heart. In order to minimize the heart damage the

cumulative dose of adriamycin will be limited. It should be noted that if the heart damage occurs it may not be reversible.

3. Bleomycin. This drug is administered intravenously. It may cause mouth ulcers and increased pigmentation of the skin (darkening of the skin). These side effects are reversible. Bleomycin may also cause lung damage when given in high doses, however, the doses of bleomycin used in this treatment plan are unlikely to cause this complication. Lung damage, however, may be irreversible if it does occur. Fever and chills also accompany the use of bleomyin in some children.

4. Cyclophosphamide. This drug is administered intravenously. It causes nausea, vomiting and hair loss, as well as depression of the blood counts. Cyclophosphamide may also cause bleeding into the urine, although efforts will be made to avoid this complication. Fibrosis (scarring) of the bladder may also occur and this effect is not reversible. Cyclophosphamide has been implicated as the cause of sterility particularly in males. Second malignancies have also occurred in patients treated with cyclophosphamide.

5. Actinomycin D. This drug is administered intravenously and may cause skin burn if it escapes from the veins into the tissues. It may also cause mouth sores, skin rashes, and depression of the blood count.

6. Cis platinum. Cis platinum is given intravenously. It causes severe nausea and may cause kidney damage, which if severe may not be reversible. Cis platinum may also cause high frequency hearing loss although this is usually of no significance.

7. Allopurinol. This drug will be given along with the methotrexate. It's side effects include nausea in a small proportion of patients and skin rashes.

All of the side effects of these drugs are reversible unless otherwise indicated.

The best therapy for osteosarcoma is unknown at this time and it is unknown whether either of the treatments in this randomized study will be superior. Your physicians feel that both of the treatments offered in this study are the best available today. Participation in this study does not preclude the use of other forms of treatment in the future should they become necessary. Your refusal to participate in this study will not adversely prejudice the care that you will receive at this hospital. You are free to withdraw from this study at any time.

In the course of this study should a new form a therapy become available which is clearly superior you (your child) will be offered the new therapy.

The Clinical Center (NCI) will provide short-term medical care for injuries resulting from my participation in this research, but neither the Clinical Center, nor the Federal Government, will provide financial compensation or long-term medical treatment for such injuries, except as may be provided through whatever remedies are normally available under law.

I understand the treatment programs and the medical aspects of my case, which have been explained to me by my NCI doctors. The NCI physicians involved in my case will make themselves available to me to answer questions I may have concerning this program. I understand that I am free to ask my physicians any questions concerning this program in the future, and that I am free to withdraw my consent to participate in this study at any time.

I understand that investigators of the Food and Drug Administration may wish to review my chart.

I have fully explained to the patient/parent/guardian the nature and purpose of the above described procedure and the risks involved in its performance. I have answered and will answer all questions to the best of my ability. I will inform the participant of any changes in the procedure or the risks and benefits if any should occur during or after the course of this study.

____
Physician's Signature

I have been fully informed as to the procedures to be followed including those which are investigational and have been given a description of the attendant discomforts, risks and benefits to be expected and the appropriate alternative procedures. In signing this consent form I agree to this method of treatment and I understand that I am free to withdraw my consent and have this form of treatment discontinued at any time without predjudice of any kind. I understand, also, that if I have any questions at any time they will be answered.

YOUR SIGNATURE INDICATES THAT YOU HAVE READ AND UNDERSTAND THE ABOVE INFORMATION, THAT YOU HAVE DISCUSSED THIS STUDY WITH THE PRINCIPAL INVESTIGATOR AND HIS OR HER STAFF, AND THAT YOU HAVE DECIDED TO PARTICIPATE BASED ON THE INFORMATION PROVIDED. A COPY OF THIS FORM IS AVAILABLE TO YOU UPON REQUEST.

Patient	Date
Parent/Guardian	Investigator
Parent/Guardian	Witness

The patient did not sign because ______________________________

______________________________ Signed

Question: To what extent is the same procedure for obtaining consent used in all cancer therapy clinics?

Answer: All cancer therapy clinics are subject to the Department of Health and Human Services regulations regarding informed consent. All patients must sign an Institutional Review Board/National Cancer Institute-supported consent form after a full explanation from their physicians.

Question: What problems are there of information transfer on drug toxicity from the laboratory to the clinic?

Answer: Before any experimental drug ever reaches human trial, it is thoroughly evaluated in animal studies in order to determine its range of side effects and suitability for use in humans. These toxicology studies form an essential part of the information base on which the human trials are conducted. It is impossible to extrapolate directly from animal findings to human toxicities. Many of the toxicities in animals are never observed in man. Thus, initial human trials of new anti-cancer drugs are conducted with specific attention to all potential side effects including those discovered in animal studies. Should new laboratory findings arise after the clinical trials have begun, then information about these findings is communicated to the investigator community through direct mailing as well as an update of the clinical brochure. The National Cancer Institute holds monthly meetings of its preclinical and clinical specialists in the area of drug toxicity in order to integrate known information about the toxicity of individual drugs. Significant new findings from these meetings are communicated to the clinical investigator community.

Question: What mechanisms are in place for improving information exchanges between the anti-cancer drug research community and the clinic?

Answer: Information is exchanged through a number of mechanisms. The National Cancer Institute holds five meetings each year of early phase clinical trials to review the results of these studies and communicate them to a larger community of physician investigators. Proceedings of these meetings are published and widely distributed. In addition, a very substantial fraction of all physicians engaged in oncologic care in the United States participates in the Clinical Cooperative Group program of the National Cancer Institute. Each group holds several plenary meetings per year at which formal presentations and informal discussions update these physicians about significant new findings on anti-cancer drugs. In addition, the National Cancer Institute is establishing a Community Clinical Oncology Program (CCOP). Among other objectives, this program will further expand the range of the information network. It is expected that several hundred community cancer physicians will be linked to the National Cancer Institute. Significant new findings that may affect the care of their patients can be distributed rapidly through this network.

Question: What progress is being made in developing anti-cancer drugs with less toxic side effects?

Answer: There are several areas where progress is being made in the development of anti-cancer drugs with less toxic side effects. In addition to our standard protocol toxicology studies, which are conducted for Investigational New Drug Application (INDA) filing with the FDA, we conduct special studies to evaluate the relative organ toxicities of different classes or groups of drugs. In this way we can select new drugs with increased margins of safety (improved therapeutic indices) while retaining established anti-tumor activity in the preclinical screening tests. Examples of the success of this approach are the development of less cardiotoxic anthracyclines (adriamycin-like drugs) and less nephrotoxic platinates (cis-platinum-like drugs).

Question: What drug is the most promising in that regard at present?

Answer: At the present, the most promising drug in this regard is probably aclacinomycin, an adriamycin-like drug which has significantly fewer side effects and promising clinical activity. Another good example would be CBDCA, a platinum-containing compound just entering clinical trials. It does not have the dose-limiting, life-threatening kidney toxicity characteristic of cisplatinum. It also appears to cause less gastrointestinal toxicity (nausea, vomiting and diarrhea), thereby improving patient comfort. The final drug that might be mentioned in this regard is Riboxamide, a new agent which should be entering clinical trials early this summer. We are excited by the prospect that it may have minimal toxicity at therapeutically effective doses. In the anti-tumor mouse screens, the drug has been very active over a wide range of doses, many of which were virtually nontoxic. In our preclinical toxicology testing we have established that it is toxic in mice and dogs only at extremely high doses. We are eager to get this promising new agent into clinical trials to evaluate its useful chemotherapeutic actions and to determine if, in fact, it is relatively nontoxic.

Question: What are the prospects for other cancer therapy approaches such as the use of interferon or hyperthermia? Would these be substitutes?

Answer: The interferons are a group of biological substances which appear to have some anti-cancer activity. Since there are several different types of interferon and within each type there may be several different molecular species of interferon, the usefulness of this family of biologics will require extensive testing. We are currently completing Phase I trials to determine the tolerated dose and toxicity of several interferon preparations. We have determined that some of these interferon preparations can be given at higher doses than was originally predicted. The side-effects have been quite predictable and appear to be self-limited. There have been some tumors which have responded to treatment and these responses are of great interest from a therapeutic point of view. Most of the responses have been partial (the tumor has not completely disappeared) and have been of short duration (a few months). However, any biologic that has anti-cancer activity is of interest. Current approaches are to confirm and extend these observations in Phase II trials to determine which cancers are most responsive to the interferons. Following would be Phase III trials, where interferon preparations are tested in conjunction with standard anti-cancer treatment to see if additive efforts could be detected. It is not currently anticipated that the interferons will substitute for or eliminate the need for other anti-cancer therapy in any particular malignancy. However, it is hoped that the interferons, being a different class of substances with different types of toxicities, might be additive and useful in the multimodality treatment of cancer. It may be several years before the exact role of these interferon preparations can be determined with respect to integration with other forms of cancer therapy.

It is highly unlikely that hyperthermia will be a substitute for the treatment of cancer by surgery, radiotherapy, or chemotherapy. Hyperthermia (raising tumors to temperatures of 43°C or higher) is expected to be most useful in complementing treatment by radiotherapy and chemotherapy. The elevated temperatures make tumor cells (and normal cells) more sensitive to radiation and to some chemotherapeutic agents. This increased sensitivity to radiation or chemotherapy may increase the cure rate for some cancers and/or reduce the risk of injury to normal organs.

Preclinical and early clinical hyperthermia research is sufficiently funded through grants and contracts. However, large scale clinical research is handicapped by the difficulty of heating tumors within the body with currently available equipment. Equipment development is being supported by private industry at this time.

PLANT PRODUCT COLLECTION

Question: We note you are phasing out your program for collecting plants that might contribute to the development of anti-cancer drugs. What was the reason for this?

Answer: The program has been ongoing for more than twenty years and although it produced compounds with novel structures for clinical trials, no compound with sufficient activity to justify a

New Drug Application (NDA) resulted from this program. In the period 1971-1980, the National Cancer Institute filed fifty-five Investigational New Drug Applications for cytotoxic agents, of which only five were for plant products. The cost of developing new fermentation and plant-derived products is significantly greater than the cost of new synthetic agents. Moreover, a large number of plant derived compounds are available by donations from interested scientists so that promising compounds would not be lost when the National Cancer Institute terminates its collection program. The National Cancer Institute will continue to work actively with scientists in this area of research to develop promising leads through the grant mechanism.

Question: Won't NCI be depriving itself of a possible good resource for the fight against cancer?

Answer: Many investigators around the world are isolating new compounds from plants as part of non-contract research. The National Cancer Institute is increasing its efforts to obtain these compounds through surveillance of the literature and personal contacts with investigators in this field. Many new plant-derived compounds can be acquired for anti-tumor testing in this way at minimal cost. Additionally, researchers may submit research grant applications to the National Institutes of Health for work on plant-derived anti-tumor agents, and such applications will have equal opportunity for funding with all other investigator-initiated grant applications. The National Cancer Institute is phasing out its targeted contract program on plant anti-cancer agents but is in no way abandoning support of this area of research.

Question: Under the new arrangements, to whom would scientists submit plants that may have promise as future anti-cancer drugs?

Answer: The Natural Products Branch of the National Cancer Institute will continue to be responsible for acquisition and screening of selected plants for anti-cancer activity in cooperation with the National Institutes of Health grantees and other collaborating scientists world-wide. A joint effort will be made between the National Cancer Institute and the scientists involved to follow up highly active leads which have the promise of leading to useful drugs.

INTERFERON

Question: The first clinical trials of interferon in this country did not appear to be very promising. To what extent is this still the case?

Answer: Many of the initial clinical trials used very impure preparations of interferons extracted from human white blood cells after virus stimulation. These preparations were difficult to purify and were only available in small quantities. Recent success in producing interferon from cells in culture and by genetic engineering has led to the availability of large quantities of highly purified interferons for clinical testing. In contrast to the interferons extracted from cells, the genetically engineered variety is not a mixture of interferons but is a single molecular species. Clinical trials are currently in progress to determine whether the mixtures seem to work better or whether the single molecular species of interferon has the activity of the mixtures. There appear to be in excess of twenty molecular species of leukocyte (alpha) interferon, perhaps two of fibroblast (beta) interferon and at least one of immune (gamma) interferon. Therefore, the clinical testing program for these interferons will be complex, in that it may be necessary to determine the toxicity and therapeutic efficacy for several of these preparations before one can make definitive statements as to the usefulness of the interferons in cancer therapy. In all trials to date, the anti-tumor responses have been seen predominantly in patients with lymphoma and to a lesser extent in patients with chronic leukemias and breast cancer. These responses have been partial (the tumor has not completely disappeared) and generally of short duration (a few months). However, Phase II trials to determine the efficacy of these interferon preparations are just beginning and it will be some time before the extent of the anti-tumor activity and its duration can be precisely determined.

Question: Is there any truth to the allegations that the interferon used in this country was freeze-dried, and thus possibly less active than the interferon used in clinical trials in Europe?

Answer: The interferons used by the Biological Response Modifiers Program have been in liquid form and there has been no evidence that they have been less active on a unit for unit basis than those previously used in Europe. Apparently, there were some feeeze-dried preparations manufactured by laboratories in Europe, subsequently used in some early United States trials by the American Cancer Society, which may have lost some of their anti-viral activity with the preparatory method used. However, this was only for one of the early types of interferon (Cantell method of preparation) and has not had any major impact on the United States trials. Moreover, we are developing and very much need to develop assays of antiproliferative activity of the interferons in addition to anti-viral activity which may be more relevant to their anti-cancer activity.

Question: If so, who was responsible for this?

Answer: The responsibility for producing freeze-dried interferon would always be that of the preparation laboratory. However, this has not been a factor in our trials.

Question: Are new trials planned for differently prepared interferon?

Answer: There are many different preparations of interferon and many more potential interferon preparations that could be tested in clinical trials. We currently are testing three types of alpha interferon prepared by extracting this interferon from either white blood cells or from cultured lymphoblasts. We are also testing genetically engineered alpha interferon. Our preparations of fibroblast interferon (extracted type) and the genetically engineered fibroblast interferon should be ready for clinical trials in 1982. We have immune interferon (extracted type) available for clinical trials in 1982 and we may have genetically engineered immune interferon (gamma interferon) ready toward the end of this year. Therefore, the National Cancer Institute's Biological Response Modifiers Program expects to conduct Phase II trials with several preparations of alpha interferon, and new

Phase I trials with at least two preparations of fibroblast interferon and at least two preparations of immune interferon. In general, where extracted forms of interferon and genetically engineered forms of interferon are both available, we are attempting to perform simultaneous testing to determine which method of producing these interferons is superior with respect to purity, activity, stability and clinical efficacy.

Question: What is the status of the production of genetically engineered interferon?

Answer: Hoffmann-LaRoche, Inc., in conjunction with Genetech Corporation, has successfully produced clone A recombinant interferon, which has been provided at no cost to the National Cancer Institute for clinical trials.

Question: To what extent is NCI involved in clinical trials of genetically engineered interferon?

Answer: We are heavily involved in clinical trials of genetically engineered interferon, having just completed the Phase I trial of a genetically engineered alpha interferon and having just begin Phase II trials with this same material. In addition, we anticipate clinical trials with fibroblast interferon from the same source and eventually with genetically engineered immune interferon, should it become available. Although we are not producing these genetically engineered interferons within the National Cancer Institute, we have developed a cooperative relationship with industry to allow combined testing of some of these materials in a cooperative program between the industrial firm and the National Cancer Institute. We would anticipate these types of relationships will be extensively utilized for the testing of other interferons and other biologics in the future.

Question: When will the clinical trials on genetically engineered interferon begin?

Answer: As described above, we have completed Phase I trials for this material and we are currently conducting Phase II trials with the genetically engineered alpha interferon. The clinical trials with other genetically engineered interferons should begin in 1982. We would anticipate that by the end of 1982, and certainly by the mid-1983, the place of the genetically engineered interferons in anti-cancer therapy will be much better defined. Hoffmann-LaRoche, Inc. has a broad clinical program for testing the anti-tumor activity of their genetically engineered alpha interferon at several institutions across the United States. It seems likely these same kinds of testing programs will be developed by the appropriate company for each of the engineered interferons. The National Cancer Institute is working with industry in a cooperative way to try to speed up this interferon testing program.

COMMUNITY CLINICAL ONCOLOGY PROGRAM

Question: There seems to be some consternation growing within the National Cancer Advisory Board about too much speed in implementing the Community Clinical Oncology Program. Please explain what's involved and what you're doing to alleviate fears within the Board about this program?

Answer: The Institute is very encouraged by the development of the Community Clinical Oncology Program (CCOP). Over the past year, the Institute has had considerable dialogue with the scientific community, including the community of practicing physicians and many advisory bodies of the Institute regarding the Community Clinical Oncology Program. Specifically, in March 1981 the Director of the National Cancer Institute announced interest in establishing a large-scale network of practicing community oncologists to participate in the National Cancer Institute's cancer control and clinical trials programs. The interest was such that the Association of Community Cancer Centers established a Committee on Clinical Research. This Committee developed a series of recommendations after holding several workshops which included obtaining the advice from fifty-five health professionals representing communities in twenty states. These recommendations and supporting documents were presented for consideration to the National Cancer Institute.

In July 1981, the Board of Scientific Counselors of the Division of Resources, Centers, and Community Activities formed a Subcommittee on Community Oncology and Technology Transfer chaired by Dr. Charles Moertel. Deliberations of that Subcommittee included academic and community oncologists, cancer center directors and cooperative group chairmen. That Subcommittee reviewed, in detail, the proposed program with a resultant approval of the concept by the full Board of Scientific Counselors in October 1981.

The Community Clinical Oncology Program has been discussed by the full National Cancer Advisory Board and the Board of Scientific Counselors of the Division of Cancer Treatment during February 1982. Future discussions are ongoing with Subcommittees of both of these advisory boards to alleviate any remaining fears that progressing rapidly with a good idea will result in a less than ideal program.

Question: To what extent will hospitals which get money under the program become permanent clients of the National Cancer Institute, requiring more and more money as time goes on?

Answer: The Community Clinical Oncology Program, when fully operational, will be a network which will allow community oncologists to participate in high priority cancer clinical treatment, control, and applied prevention trials. In its initial stages, the Community Clinical Oncology Program will be participating primarily in treatment related research. Individual programs will be monitored for quality control and, in addition, will be expected to apply and pass merit review for competitive renewal every three to five years.

FRAUD AND ABUSE

Question: We understand that the Inspector General of HHS recently examined 57 cancer contracts totaling approximately $190 million from 1978 through 1981. The study was requested to determine whether there has been any progress made since the Inspector General sharply criticized the Agency's contracting procedures in a 1978 report. The new report, according to media accounts, states that many of the same contracting problems still exist, although the Cancer Institute has made some improvements and has adopted a new plan for corrective action, (Washington Post, 11/13/81, p. A46). Why hasn't more been done to correct this problem?

Answer: The Post article is misleading since it claims that the Inspector General's report covered 1981 contract actions. Although the report is dated October 28, 1981, careful examination reveals that no files or actions taken by the National Cancer Institute after June of 1980 were included in the review. The Inspector General shared a draft with the National Cancer Institute in October of 1980. In reaction to that draft, the National Cancer Institute, National Institutes of Health and other Department of Health and Human Services units collaborated in preparation of a Corrective Action Plan, dated April 28, 1981. A copy of this Plan is included as an appendix to the Inspector General's report. It addresses specific response to each shortcoming identified and requires quarterly review and reporting. Every corrective action included in the Plan has been implemented on schedule. A February 2, 1982 review by staff of the Department of Health and Human Services Assistant Secretary for Management and Budget acknowledges that the National Institutes of Health and the National Cancer Institute have made "excellent progress" in improving contracting practices.

We have, in fact, gone well beyond improvements suggested by the Inspector General and have implemented a totally revised and strengthened management system. In addition, Institute management reviewed each of its contracts for necessity, cost and propriety and, as a result, shifted some $40 million to other high priority needs.

We believe that future audit reviews will confirm the claimed improvements in contract management since the last visit of the Inspector General.

Question: How would you rate your mechanisms for preventing waste, fraud and abuse in the use of your research funds -- effective, ineffective or in-between?

Answer: It should be made clear that the problems cited by the Inspector General exclusively involved procedural and managerial shortcomings rather than "waste, fraud or abuse". The National Cancer Institute believes that it has effective mechanisms to detect and prevent waste, fraud and abuse -- systems that are continually being strengthened and improved. As a result of effective detection mechanisms we have indeed uncovered a number of examples of improper activity, primarily involving abuse of latitude in the conduct of research. There have been extremely few cases of outright fraud perpetrated against the Institute, and the number of instances of abuse or waste has been miniscule in light of the large number of grantees and contractors using National Cancer Institute funds.

Question: What actions are taken -- and have been taken -- against individuals or institutions which do not follow your directives?

Answer: Actions are taken in direct proportion to the seriousness and culpability involved. As a minimum, the Institute always conducts or requests other qualified agencies to conduct comprehensive investigations when concerns are identified. Where problems warrant corrective action, penalties can range from extracting a promise to improve, through termination of the grant or contract, to prosecution in cases where the law has been violated. Institutions, or individuals found guilty of gross or repeated negligence might be prohibited from receiving future grants or contracts from the Department of Health and Human Services.

Question: What mechanisms do you use for detecting waste, fraud and abuse?

Answer: Techniques include the diligent and regular review of required reports; regular monitoring visits by project officers; comprehensive site visits by external peer reviewers; formal audits by trained financial or management auditors; and investigations by law enforcement agencies. The National Cancer Institute, like other National Institutes of Health components, has traditionally placed high reliance upon grantee organizations -- universities, medical schools and centers -- to share our responsibility to monitor individual recipients. During the past year we have substantially strengthened reporting requirements and placed additional emphasis on stringent monitoring by National Cancer Institute project officers. We have increased training and supervision of project officers and substantially increased funding for site visit travel.

CANCER CONTROL

Question: The budget provides a slight decrease for cancer control -- from $56.1 million in fiscal 1982 to $54.8 million in the 1983 request. In your justification you state in this regard that "new programs will be established, especially in the applied prevention area to make the program more effective." Please tell us what the problem is -- and what you have in mind for "new programs."

Answer: The National Cancer Institute has instituted a restructuring effort which will enable the Division of Resources, Centers, and Community Activities to develop and establish a number of new high priority initiatives. These activities include the Community Clinical Oncology Program which is intended to allow highly trained clinical oncologists in community practice and their patients to participate in national clinical treatment research trials. This nationwide network of community hospital-based clinical research facilities will ensure the latest high quality therapy for cancer patients close to their homes. A number of new cancer control initiatives are in the area of prevention. These studies will be conducted to obtain insight into the impact of chemopreventive agents, diet and/or nutrition on cancer incidence, as well as development of randomized case-control studies designed to quantify protective effects and to determine the potential toxicity and optional dosages of specific agents having chemoprophylactic potential.

Two other new programs that will be established in FY 1983 are the Cancer Control Research Units (CCRU) for studies of defined population and the Cancer Control Science Program. Both of these programs are intended to stimulate cancer control research emphasizing primary and secondary prevention and cancer management involving diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care. These investigations will build on the research and knowledge bases of epidemiology, biomedical, clinical, behavioral, and other sciences. The Cancer Control Research Units studies will be designed to include control groups and/or defined denominator populations in order to speed cancer control progress that may have a measurable impact on cancer incidence and survival.

INFORMED CONSENT

Question: What are the regulations concerning the use of informed consent forms? Are they being followed -- or have there been violations?

Answer: Regulations concerning Informed Consent in anti-cancer drug research are the same as those which apply to any human drug research supported by the National Institutes of Health. These regulations are specified in the section of the Code of Federal Regulations (21 CFR 50) for the Department of Health and Human Services, specifically pertaining to the Food and Drug Administration. Further federal regulations for the protection of human subjects, whether or not drugs are employed, are further defined in 45 CFR 46.

The informed consent form, which is a part of every National Cancer Institute intramural and extramural clinical trial, is reviewed by several layers of National Cancer Institute staff and approved prior to the initiation of any trial (in addition to Institutional Review Board (IRB) review and approval). This review particularly ensures that all known risks and toxicities are described. The Clinical Trials Management System (CTMS) contractor verifies that the approved form is the one actually employed throughout the trial (the extramural protocols).

As one means of ensuring that these regulations are being followed, the Institutional Review Board provides to the National Institutes of Health a certification that proper consent procedures are being followed for each project. Since January 26, 1981, when new informed consent regulations were issued, only one violation has been documented, although several complaints are currently under review.

Question: Are the toxic side effects of an experimental drug required to be mentioned on the form?

Answer: All toxic effects of an experimental drug must be fully described on the Informed Consent document.

Question: If a research hospital does not follow your directives, what actions do you take against the hospital?

Answer: When alleged violations regarding human subjects and those issues related to informed consent come to the attention of the National Cancer Institute, they are referred to the Office for Protection from Research Risks. This Office is organizationally a part of the National Institutes of Health but is responsible for implementing departmentwide regulations stipulated under 42 USC 2891-3. This section is implemented by the Code of Federal Regulations, 45 CFR 46.

CLINICAL TRIALS

Question: What actions are taken against individual researchers and their research facilities when they ignore NCI's directives on clinical trials of experimental cancer drugs?

Answer: When an apparent violation of National Cancer Institute policy or Food and Drug Administration regulations is detected, the National Cancer Institute has a range of options available. These include: 1) Repeat site visits to review a wider range of patient charts as well as procedures and policies for informed consent at that institution. In some cases after an initial site visit, it is apparent that significant changes must be made at that institution. In such instances, the National Cancer Institute may give an institution six to twelve months to thoroughly revise its procedures following which a return site visit will inspect these new procedures. 2) Actions against individual investigators include: a) suspending or removing permission to use experimental anti-cancer drugs, b) reducing or suspending funds on the grant or contract held by the investigator, c) placement of the investigators name on the National Institutes of Health Alert List, from which all subsequent applications from that investigator for National Institutes of Health funds are flagged for special consideration by both the initial review group and the National Cancer Advisory Board, and d) for especially serious infractions, the National Cancer Institute Director may recommend that the Secretary, Department of Health and Human Services, initiate debarment proceedings. This process provides for an administrative hearing which may result in removing the investigator's eligibility to compete for National Institutes of Health support for a specified time period. 3) If apparent violations of informed consent have occurred, the Office for Protection from Research Risks at the National Institutes of Health is notified. Apparent violations of investigational drug regulations of the Food and Drug Administration (21 CFR 50) are referred to the Food and Drug Administration. Further investigations for regulatory actions may be pursued by those agencies.

Question: What are your mechanisms for detecting such actions?

Answer: Research trials involving early phases of investigational drug research undergo site visits three times per year. Primary medical records as well as the informed consent records are reviewed. The National Cancer Institute is expanding its site visit program to other phases of clinical trials in which investigational drugs are involved. Certain parts of the Clinical Cooperative Group Program have been performing such site visits for several years. It is expected that the rest of the Cooperative Group Program will have a monitoring program within the next few months.

CANCER DETECTION

Question: You have been doing work on developing so-called cancer screens. What progress are you making?

Answer: Beyond the existing screens for breast cancer (mammography for women over 50 and self-examination) and cervical cancer (pap smear), there are the digital rectal exam and sigmoidoscopy. These can detect early cancer of both prostate and rectum but the exams may be difficult to administer in a screening mode. Current studies are in progress to evaluate sputum cytology for early detection of lung cancer, but it is too soon to know the value of this method. We are also evaluating the test for blood in the stool to detect early large bowel cancer and a test which samples cells from the uterus to detect early uterine cancer.

Future developments are aimed at identifying new tumor products and tumor associated substances that can be measured in body fluids such as blood and urine to provide evidence of cancers before they are large enough to give symptoms or be detected by presently available tests. There is also the possibility that certain markers will identify those individuals with a high likelihood of developing cancer so that more intensive or more frequent detection tests can be employed thereby allowing treatment to begin at the earliest possible time.

Question: Will screening for bladder cancer be possible with the discovery of a substance in the urine that signals the presence of a malignancy?

Answer: The discovery that various antigens and other substances can be present in the urine of patients with bladder cancer has not yet proven to have sufficient specificity to allow for their use in a screening program. Nevertheless, there is still reason to believe that a substance with sufficient specificity will be found as a result of new technological developments.

Question: When will such screening mechanisms be ready for application?

Answer: The evaluation of sputum cytology for lung cancer screening should be completed in three to four years. If the results are positive, it could then be applied to high-risk populations. The evaluation of blood in the stool for colon cancer screening will be completed in six to seven years. Bladder cancer screening is already being applied with cytology to identify cancer cells in the urine.

Question: What is the status of research using other bodily fluids such as spinal fluid and stomach acid to detect tumors bathed by those fluids?

Answer: Examination of the spinal fluid for the presence of cancer cells is widely used for the diagnosis of primary brain tumors and for the diagnosis of brain metastases in patients with primary tumors in other sites. In some types of brain tumors, malignant cells can be found in the spinal fluid in as many as 70 percent of patients. When leukemia involves the brain, leukemic cells can also be identified in the spinal fluid and the information on the presence and number of leukemic cells is used to guide therapy.

Research is in progress using computerized analysis of the cytologic features of malignant cells to help in the positive identification of cancer cells in body fluids. These methods should be of value in automating cytologic examinations and helping to decide whether certain abnormal cells found in the fluids are indeed cancer cells.

Fluid collected by washing the stomach can be used for cytologic examinations to identify malignant cells but it is more accurate to actually examine the lining of the stomach with a flexible gastroscope and to collect cells and tissue for diagnosis through the gastroscope. Routine screening of gastric fluid does go on in countries where the incidence of gastric cancer remains high, i.e., Japan and Finland.

CANCER TREATMENT

Question: Please describe NCI's recent efforts in using bone marrow transplants in the treatment of leukemia. Are the transplants successful in all forms of leukemia?

Answer: The role of bone marrow transplantation in the treatment of leukemia is being studied at a number of centers around the country. Briefly, the procedure involves the administration of massive doses of anti-cancer drug and/or radiotherapy in the hope that the malignant cells will be killed. These high doses would normally result in fatal toxicity because they also cause destruction of the bone marrow. To prevent this, the patient receives an injection of bone marrow from a person of similar genetic type; this marrow is usually obtained from a sibling. This transplanted marrow then "rescues" the patient by establishing itself in place of the patient's destroyed marrow.

The precise role of this procedure in the treatment of leukemia remains to be defined in acute non-lymphocytic leukemia. It is very clear that it is an effective form of treatment for this disease. Early results are extremely promising. It is not clear, however, that it is better than less toxic, simpler, and much less expensive conventional chemotherapy. The National Cancer Institute hopes to sponsor a well controlled study testing this question in the near future. Even less well defined is the role of marrow transplantation in childhood acute lymphocytic leukemia. Because of the availability of extremely effective "first-line" treatment, the procedure is performed in this disease only in patients who have undergone relapse or who are resistant to conventional therapy. Studies evaluating its place earlier in the patient's course are underway. Finally, it has been used in the accelerated phase of chronic myelogenous leukemia. Again, results are promising but still very preliminary.

Question: What new approaches for treating breast cancer are you working on?

Auswer: Probably the most important work in this regard relates to the efficacy of less mutilating surgery in the primary treatment of women with breast cancer. Ongoing trials are examining the use of segmental mastectomy with and without radiation therapy compared to conventional modified radical mastectomy, and of "lumpectomy" plus radiation. Such approaches have the potential of being cosmetically superior and of equal therapeutic benefit, as compared to conventional therapy.

Adjuvant therapy continues to evolve. Researchers are now reporting overall survival advantages, in addition to tumor-free survival, for women who receive chemotherapy following attempted curative surgery. The use of the anti-estrogen tamoxifen has proven beneficial in menopausal women. On the basis of these studies in stage II patients, new protocols for the treatment of patients with stage I disease are being undertaken.

Finally, biological response modifiers such as interferon are being evaluated. Interferon appears to be active in advanced breast cancer, but its precise role must still be clarified.

CAUSES OF CANCER

Question: In September, 1981, Dr. Robert Gallo reported isolating a virus which seems to be associated with a rare form of human leukemia. Japanese doctors have made similar discoveries. How substantial are the recently reported studies which seem to indicate that viruses are associated with certain forms of human cancer?

Answer: The recent discovery of a retrovirus ("RNA tumor virus", "Oncornavirus", "Leukemia virus") from patients with T-cell malignancies is a major breakthrough in the linkage of retroviruses to this class of neoplasia. This virus, known as HTLV, has been identified from seven T-cell leukemia and lymphoma patients at the National Cancer Institute and from one patient in Japan. Moreover, antibodies to this virus (a more rapid means of detecting presence of HTLV instead of isolation from each case) have been detected in clusters of T-cell leukemia patients in the United States, Southwestern Japan, and the Caribbean. The possible distribution of antibodies to this virus in sera of patients from other countries, especially China, Latin American countries, and the Middle East, is currently being investigated. To date, this is the only virus known to be directly linked as a cause of cancer.

Question: Which human cancers are thought to be associated with viruses?

Answer: The association of the DNA virus, Epstein-Barr Virus (EBV) with African Burkitt's Lymphoma, and with nasopharyngeal carcinoma is established. Certain other DNA viruses are also associated with human cancer. There are certain strains of papilloma virus which have been shown to be associated with some skin cancer, and hepatitis virus is associated with some hepatomas (liver cancer). There are suggestive reports of a herpes simplex virus association with cervical cancer, and of course, there is a suspicion that the recent outbreaks of Kaposi's sarcoma may be viral caused. The only known example of the association of an RNA tumor virus (retrovirus, oncornavirus) with human malignancies is that of HTLV with T-cell leukemia as described above, and this may represent not just a risk factor but a true primary cause.

Question: What are the possible applications of this new knowledge in the treatment and prevention of cancer?

Answer: Identifying viruses with specific human cancers has immediate clinical applications because it can provide a means for identifying "high risk" populations and for early detection of human tumors. From model systems, scientists have demonstrated that it is possible to passively immunize animals challenged with leukemogenic viruses. In addition, the advances in tumor immunology are compatible with developing specific antibody reagents against viruses or cells harboring these viruses, which can lead to prevention.

It might also be possible to develop biological molecules or drugs that prevent the proliferation of these viruses. Immunotherapy and immunization techniques could possibly be useful in the control of some T-cell malignancies in areas where the disease clusters. More work on understanding the mode of transmission of HTLV and other viruses described above could lead to prevention by intelligent avoidance of the source (which remains to be determined). Vaccination programs are being established for hepatitis in some areas, which could prevent liver cancers.

TRANSFORMING GENES

Question: Scientists at several institutions have found "transforming genes" in the cells of patients with leukemia, colon lung, breast, and bladder cancer. What are "transforming genes" and how do they relate to research on viral causes of cancer?

Answer: "Transforming genes" or onc genes first were identified as part of viruses. There are currently fifteen unique viral onc genes that have been identified. The extraordinary feature of these genes is that they occur in low or single copy number in the cells of all mammals. Although the normal cellular functions of onc genes are unknown, their ability, when part of a virus, to cause transformation in a wide variety of avian and mammalian species, indicates that they have an important role in cell regulation. As part of the cell, the level of onc gene expression is tightly regulated, but in the virus their expression is awry and under the control of viral transcription elements.

Among the many technologies that were developed to study viral onc genes, procedures were developed that allowed transfer of genomic or total cellular DNA from tumor cells to a certain type of non-transformed mouse cells. This routinely resulted in transfer of the viral onc gene tumor phenotype to the mouse cells and investigators immediately saw in this assay the potential for transferring human tumor onc genes. Through a quirk of nature, the human onc genes can be readily identified in the transformed mouse cells. More importantly, through recombinant DNA techniques, these genes can be isolated from the transformed mouse cells. In this and many other ways, the study of viral transforming genes has provided important technologies, which is having a profound impact on the understanding of human cancer.

Question: Are these "transforming genes" present in normal cells, and if so, how do they differ from those present in cancerous tissue?

Answer: The onc genes of transforming viruses isolated from avian and mammalian species are conserved in all mammals and are therefore present in all normal cells. Scientists at the National Institutes of Health have shown that when these genes are isolated from normal cells they do not have transforming activity. However, by adding molecular elements that switch on expression of these genes in cells, the genes become active in transformation. More than fifteen different viral onc genes have been identified. All were acquired from host genomes and several have been shown to be expressed in human tumors at what appears to be elevated levels. It may be that some of these conserved onc genes are responsible for certain forms of human neoplasia. At least four normal cell genes have been made cancerous by inserting or attaching (in vivo and in vitro) a viral transcription control element which enhances or activates expression of the transforming gene. Presumably then, certain normal cell genes have transforming potential which can be activated by transcription control elements. Chromosomal translocations, rearrangements, or mutations resulting from a variety of genetic insults, including virus infection, could cause transformation by activating or juxtapositioning a transcription control element adjacent to a normal cell gene with transforming potential.

BIOLOGICAL RESPONSE MODIFIERS

Question: Please tell us about the progress of the new Biological Response Modifiers Program. What research proposals other than those to study interferon have received funds?

Answer: In FY 1981 and in FY 1982, there began to be greater emphasis on the development of other biologics. A major priority of the Biological Response Modifiers Program (BRMP) has been the development of monoclonal antibody as a therapeutic reagent. In that regard, we have markedly increased our level of grant support in this area and we are currently exploring, through several mechanisms, monoclonal antibodies as therapeutic reagents either used alone or in conjunction with drugs, toxins or radioisotopes. A major potential advantage of monoclonal antibodies would be their specificity for the cancer cell and we are currently exploring their use as carriers to deliver targeted toxic agents to the tumor cell site. Most of these experiments are being carried out in animal tumor models but preliminary experiments have begun at some institutions in man. The BRMP supports this type of research through its grant program and we are also heavily involved with this as a research objective within our own research program at the National Cancer Institute/Frederick Cancer Research Facility. We expect to begin our own Phase I trials with monoclonal antibody to determine toxicity and level of tolerance within the next two months. These biologics will be difficult to develop since there is the potential for so many different varieties of monoclonal antibody that the testing programs for these reagents will be exceedingly complex. However, the theoretical basis for therapeutic efficacy of monoclonal antibody is strong and our program will pursue this area with a great deal of emphasis in FY 1982 and FY 1983.

We also have devoted considerable program emphasis on the development of other cell products such as lymphokines and cytokines as potential therapeutic agents. The cells of our bodies produce a variety of substances which have growth-controlling and growth-regulating effects. When these substances are active on the cells of the immunological system, they are termed lymphokines. When they are active on other cells of the body, they are termed cytokines. Interferon may be considered one of the several hundred to several thousand lymphokines that our body produces and any one of these may have therapeutic usefulness when given in a purified form in higher than physiologic doses. Cytokines include the factors which regulate cell growth normally (growth and maturation factors) and although cancer cells may be somewhat unresponsive to these factors which normally control the growth of cell in our bodies, they may still be sensitive to such factors given in pharmacological amounts (high concentrations) as a therapeutic agent. The Biological Response Modifiers Program is supporting this area of research through both grants and contracts. Although it is quite early, we intend to develop lymphokines and cytokines for therapeutic use over the next several years.

Finally, there continues to be some support available for the testing of agents which might stimulate or modulate the immune response in a direction that could be advantageous for the individual with cancer. Although this type of "nonspecific" stimulation has not been very successful in the past, there are now more purified reagents available for which some limited testing is justified. It is possible that a combination of tumor associated antigens (now capable of being isolated with monoclonal antibody technology) and a nonspecific stimulant (a drug or microbial preparation) might have usefulness as a vaccine against certain types of cancer. Therefore, the Biological Response Modifiers Program is supporting by grants and contracts some research into the isolation and purification of tumor associated antigens using monoclonal antibody technology in hopes that these can be used along with adjuvants (nonspecific stimulants) to enhance the immune response in patients with cancer and perhaps to be developed at some future time as a potential preventive agent along the lines of a specific vaccine. These programs are at a very early level of development; and while it may be years before we see progress in this area, it is an important area of research to support.

The Biological Response Modifiers Program supports investigator initiated research at the universities in a variety of different areas with a variety of different biological approaches to the treatment of cancer. It is fair to say that there is an emphasis on the part of these investigators on investigating monoclonal antibody, lymphokines and cytokines (including the interferons and thymosins), tumor associated antigens and methods of stimulating the immune response. There are many additional areas of research being investigated and there appear to be some interesting potential leads for new anticancer therapies coming from the area of biologicals.

RESEARCH MODERNIZATION ACT

Question: Have you made an assessment of how the Research Modernization Act (H.R. 556), if enacted, would affect the National Cancer Institute's budget and research efforts?

Answer: The National Cancer Institute endorses the Department's position that HR 556 not be favorably considered because it would seriously and unnecessarily unbalance the animal related cancer research programs. Enactment of this bill would severely restrict the variety of approaches to obtain objectives and thereby reduce innovative and creative scientific inquiry.

Specifically diverting 30-50 percent of animal related funding would jeopardize the promising programs of applied prevention and treatment; i.e., biological response modifiers programs, immunology monoclonal antibody studies, and metabolic pathway investigations. These programs presently rely heavily on animals. Ironically, it is these programs that will undoubtedly be responsible for shifting many existing animal studies to direct human applications.

Question: Can you provide a dollar figure on how much money would have to be reallocated as required by this bill in its present form?

Answer: It is extremely difficult to assess the exact dollar impact of this bill since the range is 30-50 percent of animal related studies. However, we estimate that approximately $50 to $90 million would need to be reallocated to comply with HR 556.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

STATEMENT OF DR. PETER L. FROMMER, ACTING DIRECTOR

ACCOMPANIED BY:

DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. JAY MOSKOWITZ, ASSOCIATE DIRECTOR FOR SCIENTIFIC PROGRAM OPERATION

ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. We will now turn to the National Heart, Lung, and Blood Institute. With us today is Dr. Peter L. Frommer, Acting Director.

Doctor, welcome again. If you will introduce your colleagues that you have with you today and give us a summary of your statement, we will go to questions.

INTRODUCTION OF ASSOCIATES

Dr. FROMMER. Thank you, Mr. Chairman. Immediately to my left is Dr. Jay Moskowitz, Associate Director for Scientific Program Operation. With us also is Ms. Evelyn Attix, Executive Officer, and on her right is John Reeder, Budget Officer.

CARDIOVASCULAR MORTALITY

It's a pleasure to be with the committee and to be able to report that the downward trend in cardiovascular disease mortality continues with us. And while it still represents more than half the deaths in the United States, since 1968 there has been a 30-percent age-corrected mortality decrease in cardiovascular disease and a 45-percent decrease in stroke mortality.

Unfortunately, in the same breath I must mention that there has been over a 40-percent increase in age-corrected mortality——

Senator SCHMITT. In what?

Dr. FROMMER. In age-corrected mortality from chronic obstructive pulmonary disease. That's really almost twice the number of deaths, before correction for changes in the number and age distribution of the population.

This is evidence that on the one hand we can do wonderful things when we have the scientific information and programs to publicize research findings, and to make the public aware; yet it illustrates also there is a great deal more to be done.

As you know, the primary mission of the Institute is the acquisition of fundamental knowledge, and this is indeed where 63 to 64 percent of our extramural funds go.

MAJOR ADVANCES

In the past year we have had a number of major advances which I'd like to call to your attention. You perhaps saw in the newspaper articles about the completion of a trial in which we demonstrated that the regular taking of beta-blocker drugs following heart attack results in a significant decrease in mortality in ensuing years.

We have seen that there is very promising research in the introduction of enzymes directly into the coronary artery involved to break up clots associated with a heart attack. This is a technique which is being increasingly widely practiced, even in some community hospitals, but without adequate validation of net benefit.

In our detailed statement, we have summarized the results of a clinical trial in which patent ductus arteriosis,. one of the most common conditions in the newborn, can be closed by the use of drugs. The need for surgery can be cut in half.

We have found in the diabetic that better management of the diabetes also better controls the level of the blood lipids which is disordered in diabetes. Whether this improves the ultimate prognosis of the diabetic, over 80 percent of whom die of cardiovascular disease, is yet to be determined, of course.

In the area of blood diseases, we have supported research proving the effectiveness of a vaccine against hepatitis B. We have new techniques for blood transfusion and blood substitutes. We have new information on sickle cell disease, on the phenomenon of gelation of sickle hemoglobin even at normal oxygen levels, long before sickling occurs.

In respiratory disease of the newborn, we have a clinical trial result, to which allusion was made this morning, demonstrating a substantial reduction in the incidence of neonatal respiratory disease. This will result in hundreds of millions of dollars of decreased intensive-care costs for the newborn.

We have also learned some of the bases for cystic fibrosis and how it affects the lung, where cystic fibrosis really does its most severe damage.

We have had major developments in diagnostic techniques—angiographic techniques including techniques that avoid the need for injection of X-ray dye into the artery and allow intravenous injection, a variety of echocardiographic techniques, methods of assessing pulmonary functions, techniques to diagnose and assess pulmonary embolism, and there are a series of techniques for separation of blood components and their characterization.

We conduct and support not only basic and applied research, but a major element of our program is the translation of findings into practical patient care. Thus, we have such demonstration programs as the national high blood pressure education program, which has been one of the major factors responsible for the decrease in stroke and heart disease mortality.

We are now in the process of adding to our health education branch programs in nutrition and, particularly, in smoking.

We have a full spectrum of research, from basic research, clinical research, the validation of research through large-scale clinical trials, to the translation of research into practice.

I'd be pleased to respond to any questions you may have.

PREPARED STATEMENT

Senator SCHMITT. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. PETER L. FROMMER

I am privileged to appear before you to recount the progress that has been made in cardiovascular, pulmonary, and blood diseases and in blood resources during the past year. It is encouraging to be able to report that the decline in deaths from heart attack and stroke in the U.S.A.--a decline that became evident in the late 1960s--continues in 1981. In spite of this promising overall trend, the toll of diseases of the heart, blood vessels, lungs, and blood continues to be large. Heart disease alone is responsible for three quarters of a million deaths each year and continues to be America's number one killer. Furthermore, the fastest rising among the leading causes of death in America is chronic obstructive pulmonary disease, a category that includes chronic bronchitis and emphysema. Chronic respiratory symptoms are now reported by one in every five persons in this country. The true impact of disorders of the blood is far greater than the death rates attributed to blood diseases. For example, blood clotting disorders underlie 90 percent of the 180,000 deaths from stroke that occur annually. The economic burden on the nation as a result of cardiovascular disease is conservatively estimated at $50 billion per year, with more than half of this attributed to hospital and nursing home services.

The magnitude of these problems remains a real challenge to the Institute, but we are able to report a number of major advances as a result of the Institute's activities. Last year, we discussed the Five-Year Hypertension Detection and Follow-up Program, a clinical trial that produced information of vital importance for millions of Americans with high blood pressure. This year I have more good news. I am pleased to report on the successful conclusion of three other major clinical trials.

The Beta-blocker Heart Attack Trial (BHAT): This past fall, the Institute announced the termination and findings of the beta-blocker heart attack trial (BHAT). This double-blind study of 3,837 patients who had suffered a heart attack shortly before the study, sought to establish whether the beta-blocking drug propranolol would reduce subsequent mortality from recurrent complications. Approximately one-half of the patients received the drug, the other half received a placebo. Although this four-year clinical trial was scheduled to continue until October of 1982, it was determined by mid-June 1981 that the trial should be stopped early because mortality in the propranolol treated group was already 26 percent lower than in the control group. BHAT clearly established a lifesaving role for beta-blocking drugs in the treatment of certain patients recovering from myocardial infarction. Although not a factor in the decision, termination of the trial 9 months early netted a savings of $2 million.

Management of Patent Ductus in Premature Infants: Four hundred premature babies with patent ductus arteriosus, one of the most common congenital heart defects and a condition usually requiring surgical closure of a major heart vessel, were randomized into three treatment groups. The first group received early treatment with the drug indomethacin; surgical closure was used as needed when improvement or closure did not occur. The second group received usual medical care early, with indomethacin given only if spontaneous closure did not occur; surgical closure was used as needed. The third group received usual medical care with surgery as needed. Surgical back-up was provided for all patients so that proper treatment was withheld from none. The results of this trial show that on discharge from hospital 70 percent of babies not receiving indomethacin needed surgical closure, but only 30 percent of babies receiving indomethacin required surgery. One-year follow-up of the babies is continuing and the final results will be reported then. It is already clear, however, that indomethacin is effective in eliminating the need for major surgery in a substantial proportion of these premature infants afflicted with congenital heart disease.

Hepatitis B Vaccine Trial: The first major clinical trial of a new vaccine to prevent type-B hepatitis is now completed. The vaccine, which provides virtually full protection against this severely debilitating disease, consists of highly purified, formalin-inactivated virus subunits, derived from the blood plasma of chronic carriers of hepatitis-B. For this study, a population of more than 1000 healthy young male volunteers at high risk of contracting the disease were randomized into two groups, one to receive the vaccine, the other a placebo. In those given the vaccine, 90 percent developed antibodies against hepatitis-B virus after two injections; this rose to 96 percent after a third injection. Of those given the placebo, less than 6 percent developed antibodies spontaneously.

Highlights of NHLBI Accomplishments

Although a major portion of the funds managed by the Institute is directed to the acquisition of new knowledge that will benefit us in the future, we are also concerned with the immediate alleviation of pain and suffering and our ultimate goal to prevent premature death in the American population. Recent accomplishments which highlight this research are outlined below:

Heart Disease Basic and Applied Research: Ten years ago, the NHLBI sponsored a Task Force on Arteriosclerosis to examine arteriosclerosis and its associated conditions, especially coronary heart disease and stroke. The Task Force recommended areas of research, development, and health care for exploration. In the decade since the original report, almost all of these recommendations have been implemented by the Institute. These activities provided new measures of prevention, control, and treatment, measures that have been incorporated into the general armamentarium of clinical medicine and public health. A new Task Force convened again in 1981 and reported on a new set of recommendations for further progress toward complete control of arteriosclerosis-related diseases.

Calcium plays a vital role in the control of heart rhythm and pump action, the muscle controlled narrowing and widening of the arteries and the storage and utilization of energy for these purposes. A new group of pharmacological agents, which block the passage of calcium across cell membranes, shows great promise for the control of abnormal heart rhythms, angina pectoris, degeneration of heart muscle, heart failure, and high blood pressure. All of these drugs, including verapamil, nifedipine, perhexiline, and diltiazem, have qualities with important implications for cardiovascular medicine.

Prevention and Education Activities: In past years, the Committee has heard about the National High Blood Pressure Education Program, a unique private-public collaborative effort administered by the Institute to facilitate more effective control of high blood pressure in the United States.

We have built upon the relationships developed with the private sector in this program to stimulate additional cardiovascular risk reduction programs at the worksite. I am happy to report that this effort is expanding and several major companies have developed related disease prevention and health promotion programs for their employees with assistance from the Institute. More recently we have emphasized work with the insurance industry which is not only instituting programs for their own employees, but also amplifying our joint efforts in prevention by promoting the programs among their numerous group subscribers. The subscribers are now adopting similar programs for their employees.

The Institute has worked with over 50 private sector organizations to promote risk factor reduction. Among these are: General Motors, Campbell Soup, Kimberly-Clark, Johnson and Johnson, General Electric, Ford, and Westinghouse. Insurance companies with whom the Institute has collaborated include Metropolitan Life, Travellers, Sentry, Massachusetts Mutual Life, and Blue Cross/Blue Shield. The Institute will continue to emphasize this effective collaboration.

Lung Diseases Basic and Applied Research: An increasing number of premature infants with Respiratory Distress Syndrome (RDS) are now being saved who may be at risk for learning disabilities later in life, probably as a result of inadequate oxygenation of the brain following failure of the respiratory system. By placing small electrodes on the surface of the scalp it is possible to record electrical signals from the brain that are generated by the reception of sound in the ear. Using this technique, investigators have now found persistent differences between signals generated by normal, full-term babies, and those from premature babies with RDS. Whether this difference represents deficits in the central nervous system, or simply a delay in development, is not yet clear, but the identification of the potential for learning disability this early in life is an important step towards better management of newborn infants and preventing potential disabilities.

Prevention and Education Activities: Asthma affects millions of children each year and continues to be the leading cause of school absenteeism. Attacks disrupt families and prevent participation in normal activities. The frequency of asthmatic attacks, however, can be reduced through self-management with the patient taking responsibility for the condition. A lack of medical compliance, failure to avoid known irritants such as dust, animals, or cigarette smoke, and inability to relax or to detect the onset, can precipitate severe attacks. The NHLBI has developed an educational program that has shown that asthmatic children and their parents can self-manage asthma successfully with a minimum of reliance on medical support. The results of a recent evaluation of the program show that children experienced significantly less school absenteeism after enrollment in the program and parents report a 66 percent decrease in related health-care expenditure.

Blood Diseases and Resources Basic and Applied Research: Perfluorochemical compounds, with a high affinity for oxygen, are showing considerable promise as one of a number of artificial blood substitutes. Research supported by the Institute has suggested a completely new possibility for the potential clinical use of perfluorochemicals. An animal model of myocardial infarction has been used to examine the effect of perfluorochemicals in the blood stream on the extent of damage to the heart. Animals treated with these blood substitutes showed only 70 percent of the heart damage experienced by controls. The Institute continues to support work on the development and use of these promising substances.

Prevention and Education Activities: In addition to basic research advances in sickle cell disease, the Institute has developed an academic tutorial program for children with sickle cell disease or trait. The program is based on the concept that children with sickle cell anemia need special help to enable them to plan and manage their lives and to reach their highest potential. Ordinary educational systems are often not sufficient in this regard, and absenteeism and academic problems result. Tutors with the program work together with administrators, teachers, parents, and agencies to encourage the afflicted child to remain in school, to develop normal friendships, and to grow in self-esteem.

The Future Prevention of Disease: The Institute views biomedical research as a broad spectrum comprising three interactive regimens: knowledge acquisition, knowledge validation, and knowledge transfer and translation. In all three regimens the focus is on prevention and amelioration of disease. In the case of coronary heart disease and stroke, for example, the identification, validation, and translation of information on the major risk factors has undoubtedly accelerated the drop in death rates from these diseases during the past decade. These results are a dramatic demonstration of the successful outcome that can be achieved with broadly based research; we shall continue to place the greatest possible emphasis on disease prevention research.

By next year vital new information about the value of reducing high blood pressure and blood cholesterol and avoiding smoking in people at high risk of cardiovascular disease, will be forthcoming from two large clinical trials of risk factor reduction. Also, in the area of secondary prevention, beta-blocking drugs and clot-dissolving enzymes will be studied to determine whether heart muscle damage can be limited during acute heart attacks. Clinical Trials: As discussed earlier, the NHLBI is committed to the support of clinical trials because this is the methodology that adequately tests the efficacy and safety of preventive and therapeutic interventions. The clinical trial is often a key step in the long, difficult, and complex process that is required to convert research discoveries into disease prevention and more effective patient care. Several trials are proposed for the future.

A new method for dissolving clots by the injection of an enzyme, streptokinase, into the arteries to the heart is dramatically relieving acute coronary obstruction. The method, however, is moving rapidly into widespread clinical use without adequate validation of net benefit and consequences, essential information that can be provided by a clinical trial. Another high priority trial is proposed to determine whether sudden cardiac death can be prevented by certain antiarrhythmic agents; a large number of drugs effectively suppress disturbances of heart rhythm, but effectiveness for saving life remains to be established. Blood clots in the lung are currently diagnosed by an invasive technique--pulmonary angiography--which carries with it a definite risk to the patient; an alternative, less dangerous method--ventilation-perfusion scanning--is now available for evaluation in the clinical setting.

Mr. Chairman, I have presented only a few of the Institute's accomplishments and future prospects. The proposed budget for the National Heart, Lung, and Blood Institute for fiscal year 1983 is $577,143,000. I thank you for this opportunity and I shall be glad to furnish any further information that you may request.

Biographical Sketch

NAME:	Peter L. Frommer, M.D.
POSITION:	Acting Director, National Heart, Lung, and Blood Institute
BIRTHPLACE AND DATE:	Budapest, Hungary (Naturalized U.S. Citizen 1947) February 13, 1932
MARITAL STATUS:	Married, 4 children
EDUCATION:	June 1954 - E.E. - University of Cincinnati, College of Engineering June 1958 - M.D. - Harvard Medical School
EXPERIENCE:	1958 - 1959 Intern, University of Cincinnati Medical Center 1959 - 1961 Staff Associate, Laboratory of Technical Development, NHLBI 1961 - 1963 Assistant Resident in Internal Medicine, University of Cincinnati Medical Center 1963 - 1966 Senior Investigator and Attending Physician, Cardiology Branch, NHLBI 1966 - 1967 Assistant Chief, Myocardial Infarction Branch, NHLBI 1967 - 1969 Acting Chief, Myocardial Infarction Branch, NHLBI 1969 - 1972 Chief, Myocardial Infarction Branch, NHLBI 1972 - 1978 Associate Director for Cardiology, Division of Heart and Vascular Diseases (DHVD), NHLBI 1973 - 1975 Acting Chief, Devices and Technology Branch, DHVD, NHLBI 1975 - 1978 Acting Chief, Cardiac Diseases Branch, DHVD, NHLBI 1978 - present Deputy Director, NHLBI 1981 - present Acting Director, NHLBI
ASSOCIATION MEMBERSHIPS:	American College of Cardiology, Fellow; American College of Physicians, Fellow; American Federation for Clinical Research; American Heart Association; American Physiological Society; American Society for Artificial Internal Organs; American Association for the Advancement of Science; Biomedical Engineering Society; Institute of Electrical and Electronic Engineers, Senior Member; International Federation for Medical and Biological Engineering; International Society for Artificial Organs.
SPECIAL AWARDS, CITATIONS, OR PUBLICATIONS:	Tau Beta Pi; Sigma Xi; Eta Kappa Nu; National Student Prize Paper, American Institute of Electrical Engineers, 1954; Distinguished Alumnus Award, University of Cincinnati, College of Engineering, 1969; Public Health Service Commendation Medal Award, 1976; Author or Co-Author of over 50 publications.

DIABETES

Senator SCHMITT. Thank you, sir.

With respect to diabetes, have you been following the trends that are leading us to more or less a duplication of the functions of the pancreas, not only in the delivery of insulin to a diabetic through insulin pumps of various kinds, but also through the use of human insulin to produce recombinant DNA technology? Do you think that will have any significant effect on reducing the cardiovascular impact of the condition of that?

Dr. FROMMER. I think Dr. Salans, Acting Director of the National Institute of Arthritis, Diabetes, Digestive, and Kidney Diseases, will be able to speak more to the details of those techniques, although I follow them with considerable personal interest. One of the things to be solved is whether tighter control of blood sugar in the diabetic will result in reduced vascular complications. The NIADDKD Institute is starting a collaborative clinical trial to test the effect of tight control on microvascular complications—complications in the blood vessels of the eye. Our clinical trials staff has been involved in the design of the study and our Institute is examining closely the possibility of being engaged in the trial, looking for effects upon the large arteries with the new noninvasive assessment techniques.

Whether closer control of blood sugar will turn out to be of clinical benefit is to be demonstrated.

CAP ON INDIRECT COSTS

Senator SCHMITT. Do you have anything to add to the comments made earlier about the effect of the cap on indirect costs for research grants?

Dr. FROMMER. I think it's important to alert the community in general that it is time to take a careful look at what are the constituents that go into the indirect costs.

We send a full team of scientists to look in great detail at the need as well as the financial aspects of the direct costs we pay. For the indirect costs we pay, only accountants are involved and these costs are examined only according to accounting principles and rules. Our role in indirect costs is being reviewed, and appropriately so.

BUDGET CUTS

Senator SCHMITT. Are there any unique aspects to your Institute that have come to light with the budget cuts and attempts to cut administrative costs over the last year?

Dr. FROMMER. No; basically we face similar problems of trying to achieve as much as we possibly can, utilizing efficiencies wherever possible, to make the dollar go further, trying to get more research out of our resources.

RESEARCH CENTERS

Senator SCHMITT. How much are you spending on research centers in fiscal year 1982, and what do you expect to spend in 1983?

Dr. FROMMER. In research centers in 1982 we are spending approximately 16 percent of our extramural budget; in 1983 we expect to be spending $70 million for research centers.

Senator SCHMITT. You said 16 percent in 1982?

Dr. FROMMER. That's correct.

Senator SCHMITT. Which is about 64——

Dr. FROMMER. It's a little less than 16 percent, Mr. Chairman, because that also includes some other grants in response to requests for grant applications. In 1982 the funds for research centers is $64,800,000, and $70,100,000 in 1983.

Senator SCHMITT. Do you see any possible economies that can be achieved here without compromising essential research and treatment activities?

Dr. FROMMER. Not really. The figures here are deceptive. This is not growth in the program. It is because in fiscal year 1982 we are taking some savings that have accumulated in some of the programs. So these centers are actually functioning at a higher operational continuation than the $64 million level because of the application of previous years' savings. That's the reason there is this apparent anomalous $5 million increase.

What you see here for fiscal year 1983 represents a decrement of approximately 4 percent below the previously committed funding level.

ARTIFICIAL HEARTS

Senator SCHMITT. Do you have any comments about the future utilization of artificial hearts?

Dr. FROMMER. Certainly this is one of the most interesting and challenging topics——

Senator SCHMITT. Other than those your wife or girlfriend might have made. [Laughter.]

Dr. FROMMER. Our primary goal of research in heart disease is prevention. Our second goal is forms of therapy which are widely applicable because of their economy and utility. Nevertheless, artificial hearts or auxiliary pumps—in other words, a device that is added into the chest but does not replace the heart—have their place in our program. These activities are moving forward at a very satisfactory rate. I'm quite sure that they will be technically successful, and there are certain patients for whom they will mean the difference between life and death.

We are designing them to provide a good quality of life—at least 2 additional years of relatively normal ambulatory activities. One will need to recharge the external batteries once, maybe twice, or even three times a day. This will be a solution which may be valuable to a relatively small but still a significant number of people.

CORONARY ARTERY SURGERY

Senator SCHMITT. I have been told that it has been estimated that coronary bypass surgery constitutes 1 percent of the total costs of the national health care overall. Do you agree with that? Do you have any reason to disagree with it?

Dr. FROMMER. I think it costs that much or a little more.

Senator SCHMITT. Do you think it's abused or overused relative to other alternatives?

Dr. FROMMER. We are in the process of a large-scale study of coronary artery surgery. We have a study in which we have collected data from 25,000 patients from 15 institutions. Between 1975 and 1979 almost all patients at these hospitals who underwent coronary angiography, which is a final diagnostic step before coronary bypass surgery, are entered in the study. From these 25,000 patients, and from a subset of 780 patients who are participants in a randomized study, comparing medical against surgical therapy, we will be getting results which are more definitive.

At this point in time, we have to go on the basis of the information which is available from other sources.

Coronary bypass surgery has to be looked at from two major points of view: What it does to the length of life and what it does to the quality of life.

With respect to length of life, there are very fine data which prove that for patients who have what is called left main coronary narrowing—that is, that part of the coronary arteries which nourishes most of the heart—there is a very substantial improvement in life expectancy. However, this represents no more than 5, maybe at the most 8 or 10 percent, of the patients who undergo bypass surgery.

There are some data which suggest that bypass surgery may improve life expectancy in patients who have significant disease of all three of the major coronary arteries. The consensus we got on this topic in December 1980, indicate that while these data were impressive, they needed corroboration from larger scale studies, which is what we have now in progress.

For most other patients at this time, it is probably generally not so much a matter of saving of life as it is improving the quality of life. And there is no question but that there are many, many patients who would otherwise be completely incapacitated were it not for the bypass procedure.

Having said all that, I'm also sure that there are many patients who have coronary bypass surgery in whom the medical management—advice on life style, choice and optimal dose of medications, allaying of fears, and other aspects of medical management—have not been handled as fully as they might have. That is to say, for some of these patients very significant improvements in quality of life could have been achieved without surgery.

I cannot say if the number of bypass procedures is too great or too low. I'm sure that there are some patients I would not have sent to surgery who have gone, and I'm sure there are others who should go and who haven't gone.

Senator SCHMITT. Do you think both numbers are significant? That's very easy to say. I'm sure you're right.

Dr. FROMMER. I think they are both significant. But you have to appreciate that there are many physicians, expert cardiologists, and there is a spectrum of judgments. We sought to explore this, to pull this together, and we have a consensus report on this which we have widely disseminated. I would be pleased to submit it for the record.

Senator SCHMITT. We would like to have that.

Do you suspect that the number who don't need it is not the same number that do that don't get it?

Dr. FROMMER. I will know much more about the number who need it when the trial we now have is completed. That is because it will give us some results from randomized studies which will tell us about life expectancy. When those trials are completed—we now estimate it will be late in 1983—we should have better data.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH

CONSENSUS DEVELOPMENT CONFERENCE STATEMENT

CORONARY ARTERY BYPASS SURGERY: SCIENTIFIC AND CLINICAL ASPECTS

December 3-5, 1980

A Consensus Development Conference was held at the National Institutes of Health on December 3-5, 1980 to consider the status of coronary artery bypass surgery in relation to five specific questions:

1. What is the overall management of coronary artery disease--that is, in what context should coronary artery surgery be considered?
2. What constitutes a reasonable diagnostic workup before recommending medical or surgical therapy?
3. What is known about long-term survival after coronary artery bypass surgery in specific patient groups?
4. What is known about long-term quality of life after coronary artery bypass surgery?
5. What is the range of success rates for the procedure in various settings, and what factors may be important in influencing this outcome?

1. What is the overall management of coronary artery disease--that is, in what context should coronary artery surgery be considered?

Coronary heart disease may be recognized by the physician as the clinical syndromes of angina pectoris, acute myocardial infarction, sudden cardiac arrest, or ischemic cardiomyopathy. It may also be recognized in an asymptomatic form by detection of electrocardiographic evidence of prior myocardial infarction not recognized during the acute episode or by characteristic abnormalities of the electrocardiogram during testing of apparently healthy persons. Once suspected by the physician, the diagnosis may be confirmed with various levels of certainty by one or more special diagnostic tests. The tests most commonly used include the electrocardiogram recorded during and after monitored graded exercise, in some institutions radionuclide studies of myocardial perfusion and ventricular function at rest and in response to exercise, and coronary arteriography with left ventricular angiography. In addition to confirming the diagnosis, such studies may provide information about the pathology and anatomy of the coronary arteries, the functional condition of the left ventricle, and the overall response of the circulation to stress. These data may be combined with those obtained from the medical history and physical examination and with detailed knowledge of the natural history of the disease derived from many long-term follow-up studies of patients having such tests, to form definable subsets of persons with widely different prognoses. Since a fundamental aspect of advanced coronary heart disease is a greatly increased probability of sudden death or myocardial infarction, such prognostic information strongly influences the decision of whether to add coronary artery bypass surgery to the overall lifelong medical management recommended.

If the combined data indicate that the patient is at high risk of sudden death or infarction for example, if the patient has severe stenosis of the main trunk of the left coronary artery or severe and proximal stenosis of multiple major coronary branches--surgery is given especially serious consideration. On the other hand, if the studies indicate no critical stenosis of any major coronary branch, surgery is clearly not indicated and medical treatment is advised.

A very large percentage of patients fall between these extreme examples. In these patients, recommendations for medical or surgical therapy are based on two fundamental questions. The first question, often the most anxiety provoking to the patient, relates to which course will provide the greatest protection from disabling myocardial infarction or death. The second question relates to which course will permit a satisfactory quality of life according to the patient's own standards. The answers to these questions are highly judgmental. The answer to the first is largely based on the physician's interpretation of a large volume of sometimes contradictory data of extraordinary complexity. The answer to the second is largely based on the individual response to medical therapy and on the patient's priorities.

It is common practice for the physician and patient, when faced with this problem, to initiate comprehensive medical therapy with subsequent periodic reevaluation of the intervention based on the patient's response to his treatment. It is critical to recognize that appropriate, comprehensive medical care of the patient with coronary heart disease requires an intensive effort on the part of the physician, involving consideration of almost every aspect of the patient's life. It requires careful education of the patient and spouse on the nature of the disease and its management as to allow adequate selfcare on a continuing basis and to allow the patient to participate knowledgably in major decisions affecting his or her life. It requires optimal control of risk factors for atherosclerosis and modification of the patient's lifestyle. This may affect both work and leisure activities. It may require long-term administration of such potent medications as nitroglycerin, beta-adrenergic blocking drugs, long-acting nitrates, antiarrhythmic agents, and digitalis. Effective and safe use of these therapeutic agents requires careful titration of dosage according to subjective and objective indices. If, after such careful and intensive medical treatment, the patient believes that the quality of life is so adversely affected that other alternatives must be sought, then surgical therapy may be advised. It must also be recognized that in many cases dissatisfaction with the altered life style imposed by the illness is the result of inadequate attention to the details of management; failure of the physician to educate the the patient concerning appropriate use of the indicated medications may be a particularly important cause of this outcome.

In patients with chronic stable angina and good ventricular performance, the operative mortality associated with aorto-coronary revascularization of the heart, whether with autologous vein or artery, has progressively declined to 1 to 2 percent at major surgical centers. A corresponding decrease in perioperative myocardial infarction has been achieved. These results are assumed to relate to better management of anesthesia, more complete myocardial revascularization, and improved methods for protecting the heart during the period of coronary grafting. There seems to be no doubt that coronary bypass can improve myocardial perfusion. The patency of aorta-coronary saphenous-vein grafts has been 80 to 85 percent two years after operation. The procedure has been widely accepted for patients receiving medical therapy who have unacceptable symptoms and for certain other subsets of patients with coronary artery disease.

2. What constitutes a reasonable diagnostic workup before recommending medical or surgical therapy?

A reasonable diagnostic workup of a patient with angina pectoris depends upon the clinical problem at issue. Instability and severity of angina, effect of the disease on the quality of life, cardiac function, and to a certain degree, age are all important in determining the workup of each patient. The workup should be done as efficiently as possible to provide definitive information on which clinical decisions can be based. Unnecessary and redundant procedures should be avoided.

In some patients the clinical picture indicates that definition of the coronary anatomy is needed to determine operability. It is agreed that patients with stable angina whose quality of life is significantly impaired by their symptoms should undergo coronary arteriography. Further, in patients with unstable angina, coronary arteriography should be performed during the initial phase of hospitalization; if maximal medical therapy does not relieve symptoms, this procedure is considered urgent. There is consensus that coronary artery bypass is indicated in patients with unacceptable symptoms during appropriate medical treatment or with recurrent unstable angina, but the decision to operate must also depend on the results of invasive studies.

In patients with typical angina not sufficiently severe to dictate surgery for relief of symptoms, noninvasive cardiac testing may be carried out initially in an attempt to identify those at high risk for major cardiac events. However, there is lack of consensus on the value of noninvasive testing in the workup of such patients. Some physicians perfer coronary arteriography as the initial diagnostic procedure, particularly in the young patient. Others recommend exercise electrocardiography to identify patients with serious left main coronary artery or triple-vessel disease. Such patients will often have early or excessive ST-segment deviation, prolonged ST segment depression in blood pressure during the test. In this category of patients coronary arteriography should be carried out, and if high-risk disease is found, coronary artery bypass surgery should be considered. The use of radionuclide studies to identify high-risk patients with left main coronary artery or triple-vessel disease needs further evaluation.

There is a lack of consensus on the approach to evaluation of patients with questionable or atypical angina. Exercise electrocardiography may be helpful in identifying those with serious coronary disease; such identification may be enhanced by radionuclide studies in conjunction with exercise testing, particularly in patients with resting electrocardiographic abnormalities that impair interpretation of the exercise electrocardiogram. The presence of coronary artery disease may be indicated by transient effects in myocardial perfusion, by wall motion abnormalities, or by an abnormal response of the left ventricular ejection fraction to exercise. Further research is needed to determine the role of noninvasive testing when the presence of coronary artery disease is known or suspected.

Survivors of an acute episode of myocardial infarction are at high risk of sudden death during the first year after the infarction. Recent studies have demonstrated that one year mortality ranges from 10 to 15 percent of all survivors. Several investigators have reported that these patients can be divided into high-risk and low-risk subgroups on the basis of clinical information and such noninvasive testing as exercise electrocardiography, radionuclide studies of ventricular function, and ambulatory 24-hour electrocardiographic recording. It is believed that high-risk patients should undergo coronary arteriography and left ventricular angiography followed by surgical intervention if the coronary anatomy and left ventricular function are approriate. It should be recognized, however, that the course of these patients undergoing surgery may differ from that in patients with stable or unstable angina and apparently similar coronary anatomy and ventricular function, in that the former group appears to have a greater tendency toward major ventricular arrhythmia. It is also recognized that there are insufficient data to determine whether surgical intervention will reduce mortality in this special subset of patients with coronary heart disease. Because of the relatively large number of patients included in this high-risk post-myocardial infarction subset and the present uncertainty about their proper management, there is an urgent need for further investigation of this problem.

The problem of the patient with coronary disease presenting with congestive heart failure needs special consideration. It is important to determine whether a lesion amenable to surgery is contributing substantially to the heart failure--e.g., a ventricular aneurysm, severe mitral incompetence, or a ventricular septal defect resulting from myocardial infarction. Twodimensional echocardiography or radionuclide ventriculography may be helpful in the evaluation of such patients.

3. What is known about long-term survival after coronary artery bypass surgery in specific patient groups?

The impact of coronary artery bypass surgery on the survival of patients with coronary artery disease has been the focus of extensive debate since its introduction. Severe left ventricular dysfunction has been determined to have an adverse effect on survival, and comparisons between surgical and medical therapy must take this into account, as well as the anatomic location and extent of disease defined by coronary arteriography.

The difficulty of interpreting the results of surgical series by comparison with historical controls is well recognized. This type of comparison is especially hazardous in the assessment of coronary artery surgery because of marked differences between early and recent results for both surgically and medically treated patients. Several recently published series with long-term follow-up of patients undergoing coronary artery bypass have documented an impressively low operative mortality with a remarkable long-term survival. At the same time, other studies have noted a marked improvement in recent years in the survival of medically treated patients. Accordingly, it seems unlikely that the benefits of surgery, even in appropriately defined subgroups, can be assessed from studies that are not adequately controlled.

It is agreed that in patients with angina pectoris and more than 50 percent narrowing of the luminal diameter of the left main coronary artery, bypass surgery results in better survival than medical treatedment, regardless of left ventricular function or the degree of angina pectoris. Survival rates after medical and surgical therapy were 60 and 89 percent, respectively, at four years in the Veterans Aministration trial, and 67 and 89 percent, respectively, at five years in the European trial. Left main coronary artery stenosis of this severity is present in approximately 10 percent of patients undergoing coronary arteriography. (Since estimtes of the prevalence of lesions based on coronary angiography depend on the criteria for angiography, considerable variability may exist among individual institutions.)

There are only a few prospective randomized trials and observational studies with concurrent medically treated controls for use in assessing the impact of surgery on survival. Furthermore, such results must be applied with caution to the overall population with symptomatic coronary artery disease treated in a variety of centers. This situation compounds the problem of judging the effects of coronary artery bypass on survival in patients with three-vessel disease, for whom conflicting data exist. Three-vessel coronary artery disease of surgical importance has been reported in 30 to 40 percent of angiographic studies. The initial report on the Veterans Administration Cooperative Randomized Trial did not demonstrate improved survival with surgery in patients with three-vessel disease, the majority of whom had moderate impairment of left ventricular function. However, if one accepts the analysis of the Veterans Administration data for the 10 hospitals (including 87 percent of the patients) in which the average operative mortality was 3.4 percent and eliminates the three outliers in which the average operative mortality was 23 percent, a substantially improved survival with surgery is observed. Evidence from some observational studies suggests improved survival in patients with three-vessel disease and moderate impairment of global left ventricular function, i.e., left ventricular ejection fraction in the range of 25 to 50 percent.

Data were reviewed that suggested improved survival after coronary artery grafting in patients with three-vessel disease and good left ventricular function, defined as left ventricular ejection fraction greater than 50 percent. The European Collaborative Randomized Trial has demonstrated improved survival for surgically treated patients in this subset. Although the differences observed in the European trial are impressive (the survival rate at 60 months was 82 percent for the medical group and 94 percent for the surgical group), there is consensus that confirmation of these findings in additional studies is needed before a firm conclusion can be reached on the question of improved survival in patients with three-vessel disease and good left ventricular function as defined above. Other smaller randomized trials and observational studies have yielded conflicting results in this subset.

The two large randomized studies examined do not provide evidence of improved survival with surgery in patients with two-vessel disease, regardless of the status of the left ventricle, but some observational studies have suggested improvement in survival with surgery of patients with two-vessel disease and moderate impairment of left ventricular function. There is no evidence of improved survival after surgery in patients with single-vessel disease, regardless of left ventricular functional status.

The available data are not considered adequate to support the conclusion of improved survival with surgery in patients with severely impaired left ventricular function, i.e., left ventricular ejection fraction less than 20 percent.

The National Heart, Lung, and Blood Institute Multicenter Randomized Unstable Angina Pectoris Trial, which excluded patients with left main coronary artery disease or persistent unstable agina, has failed to show improved survival of patients treated by urgent surgery, as compared with those treated exclusively by medical management, unless surgery was dictated by chronic symptomatology. The extent to which the results in this highly selected group of patients can be extrapolated to other patients with unstable angina has not been established.

It is important to reemphasize that surgery may still be appropriate in patient subsets in which evidence of improved survival with surgery is lacking, if symptoms of myocardial ischemia are sufficiently severe or if large areas of myocardium are in jeopardy. Further attempts should be made to identify other variables, currently unmeasured, that may affect survival and thus provide methods for more critical testing of therapeutic effectiveness.

4. What is known about the long-term quality of life after coronary artery bypass surgery?

There are few objective criteria by which quality of life can be assessed following coronary artery surgery. The symptom of angina pectoris is reported to be relieved in 80 to 90 percent of patients undergoing surgery for chronic stable angina. Bypass has reduced the subsequent number of cardiac-related events, the amount of medication required, and the frequency of hospitalizations. The majority of patients have been able to increase their exercise capacity and improve their New York Heart Association functional class after operation. This observation has been documented by improvements in functional exercise testing, angina threshold, left ventricular wall motion, left ventricular ejection fraction during exercise, indexes of myocardial oxygen consumption during exercise and lactate extraction across the myocardium.

Theoretically, improvements in symptoms and functional capacity associated with coronary bypass should enable more patients to resume gainful employment. The consensus is that this expectation has not been realized. It is recognized that physicians do not make consistent recommendations to patients regarding exercise potential and employability after successful coronary surgery. Factors extraneous to the patient-physician relationship, such as preoperative work status, availability of other income, perception of health, age, level of education, and employer attitudes, all appear to influence the postoperative employment status. Whether or not the patient returns to work after coronary surgery depends on too many nonmedical factors to allow any conclusions regarding efficacy of therapy based on this characteristic.

It is reported that angina will recur or progress after bypass surgery in about 5 percent of patients per year. In approximately two-thirds of these patients, symptoms are related to closure of the vein graft or progression of disease in the native circulation.

This may be related to persistent elevation of blood lipids or poor control of other risk factors. The mechanisms involved in progression of atherosclerosis in the coronary circulation and in grafts are important and require further investigation.

Similar results regarding quality of life have been observed in patients undergoing coronary bypass for unstable angina, but the reported follow-up data cover a shorter period than those cited, which are based predominantly on patients with stable angina.

5. What is the range of success rates for the procedure in various settings, and what factors may be important in influencing this outcome?

The institutional setting in which bypass grafting is performed may have an important influence on the success of the operation in various clinical subgroups. Excellence can be achieved in a variety of hospital settings, provided that appropriate medical and technical support is available to complement an experienced and skilled surgical team. The necessary features include expertly performed angiography in suitably equipped laboratories, the availability of other subspecialty resources, and appropriate laboratory and blood-banking facilities.

Successful intraoperative management--reflected in low rates of mortality, perioperative infarction, and other postoperative complications--and short hospital convalescence will depend not only on surgical skill and judgment but also on the availability of competent anesthesiologists, efficient extracorporeal support, optimal myocardial preservation techniques, and a minimal period of myocardial ischemia consistent with optimal revascularization.

Postoperative management requires a suitable intensive-care facility, dedicated personnel and the availability of circulatory support systems.

With the experience that has been accumulated to date, the following hospital mortality and perioperative infarction rates can be expected.

In patients with chronic stable angina pectoris and normal or moderately impaired left ventricular function, a hospital mortality rate of 4 percent is generally attainable, and a rate of less than 1 percent is possible. The incidence of electrocardiographically documented perioperative infarction may approximate 5 percent.

In the syndrome of unstable angina pectoris, early results will depend upon the institution's approach to management. A somewhat higher incidence of morbidity and mortality may result from earlier operative intervention, and lower risks may result from a longer period of stabilization and exclusion of patients with evolving infarctions. With initial stabilization and nonemergency operation, hospital mortality and perioperative infarction rates should approach those in patients with chronic stable angina pectoris. Even with early intervention, a hospital mortality of 6 percent is generally attainable, and perioperative infarction may approximate 10 percent.

Left main coronary artery involvement has been associated with high operative risks in the past. Except under emergency conditions, patients with this lesion can be treated surgically with morbidity and mortality rates only slightly higher than those in patients with chronic stable angina and a different coronary anatomy.

Bypass grafting in patients with severe left ventricular dysfunction has been associated with high operative morbidity and mortality. Recent improvements in perioperative management has lessened the risks. In patients with very severe myocardial dysfunction--that is, ejection fractions of less than 25 percent--a hospital mortality rate no greater than 15 to 20 percent is generally achievable.

At present there is insufficient information to identify the role of bypass surgery in patients with acute myocardial infarction or intractable ventricular arrhythmias, or in asymptomatic patients with jeopardized myocardium.

For all categories of patients, an average one-year graft patency of 85 to 90 percent should be achievable. The roles of anticoagulant and antiplatelet therapy, as well as other interventions that may affect late graft patency and retard the arteriosclerotic process, are not known at present and require further study.

Conclusion

There is consensus of the panel that coronary artery bypass represents a major advance in the treatment of patients with coronary artery disease. Evidence has been presented to support the conclusion that an improvement in the quality of life, a decrease in myocardial ischemia, and an increase in survival have been demonstrated after coronary artery bypass in selected subsets of patients.

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Robert L. Frye, M.D. (Chairman), Chairman, Division of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota

W. Gerald Austen, M.D., Chief of Surgical Services, Massachusetts General Hospital, Boston, Massachusetts

Paul A. Ebert, M.D., Professor and Chairman, Department of Surgery, University of California, San Francisco, California

Charles K. Francis, Jr., M.D., Assistant Professor of Medicine, Co-Director, Cardiac Catheterization Laboratory, Division of Cardiology, Yale University School of Medicine, New Haven, Connecticut

Nicholas T. Kouchoukos, M.D., Professor of Surgery, University of Alabama in Birmingham, Birmingham, Alabama

Paul Meier, Ph.D., Department of Statistic', University of Chicago, Chicago, Illinois

Hiltrud S. Mueller, M.D., Professor of Medicine, and Chief of Cardiology, St. Louis University School of Medicine, St. Louis, Missouri

Elliot Rapaport, M.D., Professor of Medicine, University of California, San Francisco, San Francisco, California

T. Joseph Reeves, Director, Cardiovascular Laboratory, St. Elizabeth's Hospital, Beaumont, Texas

David C. Sabiston, Jr., M.D., Professor and Chairman, Department of Surgery, Duke University Medical Center, Durham, North Carolina

William C. Sheldon, M.D., Chairman, Department of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio

Robert L. Vitu, M.D., Saginaw, Michigan, Assistant Clinical Professor of Family Practice, College of Human Medicine, Michigan State University, East Lansing, Michigan

James H. Ware, Ph.D., Associate Professor of Biostatistics, Harvard School of Public Health, Boston, Massachusetts

Special participants in the discussions of the Panel included the following:

Samuel Gorovitz, Ph.D., Chairman, Department of Philosophy, University of Maryland, College Park, Maryland

David C. Levin, M.D., Associate Professor of Radiology, Harvard Medical School, Boston, Massachusetts

William B. Stason, M.D., Associate Professor of Health Policy and Management, Harvard School of Public Health, Boston, Massachusetts

ALCOHOL AND CARDIOVASCULAR DISEASE

Senator SCHMITT. What is the prevailing wisdom now on the effect of small amounts of alcohol on the functioning of the cardiovascular system—an ounce a day keeps the apple away, or whatever. [Laughter.]

I never could get it.

Dr. FROMMER. Well, I think the prevailing wisdom is that there is much greater hazard in an ounce leading to 2 ounces and 4 ounces, and all the hazards and damages from that, than the very small benefit that would seem to have been shown in some epidemiological studies indicative that those who drink one drink a day on the average have a slightly lower mortality rate than those who abstain completely.

In all fairness, we have to say there is a physiological or biochemical rationale that one could explain this benefit. Alcohol raises the high-density lipoprotein cholesterol, and this is the component of cholesterol that seems to be somewhat protective against heart disease.

But I certainly don't go around advising people to have a drink a day to keep the doctor away.

Senator SCHMITT. So you're saying they are dying of liver disease with perfect coronary arteries. They're still dying. [Laughter.]

Dr. FROMMER. Very well put. Furthermore, as one increases the alcohol consumption, the liver, the brain——

Senator SCHMITT. Car accidents.

Dr. FROMMER. Car accidents.

CARDIOVASCULAR RISK FACTORS

Senator SCHMITT. What about other of my so-called bad habits? Is that really the main enemy that you're fighting out there, given everything else—bad nutrition, bad exercise, or smoking?

Dr. FROMMER. The largest health publicity campaign that we have mounted has been on hypertension, and we are now in the position that since 1972 when the NIH started its program, there has been a precipitous decline in those conditions most directly related to hypertension. The mortality rate from stroke has decreased more than 5 percent each year since that time. Similarly, we have had a decrease in heart disease deaths of about 3 percent per year.

So, certainly, we are concerned about blood pressure. We are now finding that, whereas a decade ago about 16 percent of the people who had high blood pressure were really controlled adequately on drugs, the most recent surveys suggest it's close to 50 percent.

Senator SCHMITT. Are those drugs substitutes for exercise, Dr. Frommer?

Dr. FROMMER. Let's look at it the other way. Exercise can be a substitute for drugs in many. The withholding or rather the reduction of salt intake can be another important step. Maintenance of ideal body weight can be very important.

Each of these is important. There are other techniques we are looking at—and they are very important to look at—because we would hate to think of literally 40 million, maybe 60 million, Americans on drugs for the rest of their lives. It is a very scary thing. Most of all, we need research leading to the primary prevention of hypertension, not just better treatment.

That concerns only high blood pressure.

We are very concerned with smoking, of course. We often call attention to the devastating effects of smoking in causing lung and other cancers. However, there are other unequivocally devastating effects of smoking upon the lungs—tobacco and marihuana as well. Cigarette smoking tears the lung apart. Chronic obstructive pulmonary disease is at least 10 times as common in the smoker as in the nonsmoker; it is the fifth leading cause of death and the most rapidly increasing cause of death. And the real tragedy is that by the time one can measure the decrement in pulmonary function by easily available techniques, the patient is already on an irreversibly downhill slide; one can only retard the rate of damage, not stop it.

What we'd like to do is develop techniques for detecting subtle derangements of lung function so we can better motivate the smoker to stop smoking.

And, of course, cigarette smoking doubles the risk of coronary heart disease.

In the area of exercise, we put out a booklet to help people exercise. It was so popular that Good Housekeeping copied it almost verbatim, and included it in its January 1982 issue. We are very pleased with that.

With respect to nutrition, we feel that the problem is a bit more difficult because one cannot give as universal advice to everybody. It's safe to say that Americans on the whole consume more salt than is necessary or desirable, or that Americans on the whole have higher blood cholesterols than is ideal, and they can decrease their blood cholesterol by the food they eat, by losing weight, and exercise. But we have to be careful with any nutrition messages because all the facts are not in, and there is not a universal, simple, and unequivocal message. We have to be careful that what is a prudent message suitable for most Americans is not presented as a marching order for all. We have to be very careful in laying out what is and what is not known. We look forward to data forthcoming from several clinical trials nearing completion. As further information becomes available, we want to be able to communicate sound nutrition messages.

ARTIFICIAL BLOOD

Senator SCHMITT. How do we stand on artificial blood?

Dr. FROMMER. Artificial blood has evolved out of a research program started by Dr. Lee Clark of Cincinnati and supported by this Institute over 15 years ago, and very substantial progress has been made. Over a dozen patients in the United States have had this artificial blood, patients who were Jehovah's Witnesses, and who for religious reasons could not accept blood transfusions, but who critically needed surgery. This blood substitute has been used in Japan in several hundred patients. We are in the process of looking for more highly purified substances where we can be increasingly sure of safety. The potential use of artificial blood is much broader than its U.S. use to date. It may be a wonderful way of storing "blood" for massive emergency needs, for example.

It is also interesting that the blood substitutes can also serve as a research tool. This is a good example of the interrelation between clinical application and fundamental research. If an animal is exsanguinated and its blood replaced by a blood substitute, we find the animal does not bleed. So the clotting factors in blood are not the only factors preventing bleeding. Such an animal is also a wonderful way of looking at how blood constituents—the formed elements, clotting factors, nutrients, enzymes, and so on—return into the circulation. It is useful for a variety of other physiological studies as well.

POTENTIAL GROWTH

Senator SCHMITT. Do you think you get more bang for your buck than the Institutes that have a higher growth rate in their budget? Do each of your grants cost less? Do you have easier research problems or less expensive, if not easier?

Dr. FROMMER. That's a loaded question.

Senator SCHMITT. I never ask loaded questions. [Laughter.]

Dr. FROMMER. I think each of the Institute Directors and Acting Directors would say that we could very well utilize additional dollars very effectively.

Senator SCHMITT. Yes; but you have grown more slowly than some of the other Institutes, and I'm just curious: Has that affected the progress in this area? You are covering the areas that at least in aggregate account for most of the deaths by natural causes, so-called, in the country.

Dr. FROMMER. Yes, over 50 percent of the deaths, over 30 percent of the health-care dollars. We certainly feel that there are a number of clinical trials, a number of other targeted research projects and, of course, investigator-initiated grants that we would very much like to do if we had the funds. But this is a time when there has to be a very tight allocation of funds and a critical balance.

Senator SCHMITT. So your objective judgment is the distribution between the Institutes is just about right? [Laughter.]

Dr. FROMMER. You said that, Senator; I didn't. [Laughter.]

SUBMITTED QUESTIONS

Senator SCHMITT. Thank you, Doctor. We appreciate it. And we will have some questions for the record.

Dr. FROMMER. Thank you.

Senator SCHMITT. Keep up the good work.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

BUDGET POLICY

Question: The budget proposes to cap indirect costs for research grants at 90% of actual cost and also to reduce the average cost of non-competing continuation grants by 3 to 4 percent; and to maintain training allowances slightly below the Fiscal 1982 Level. What will these policies do to your research and training efforts?

Answer: The impact upon NHLBI research and training efforts will be similar to that of the impact of these changes in other Institutes. Indirect costs for research grants would be capped at 90 percent of actual cost; all research grants would be reduced in the range of 3 to 5 percent, not just non-competing continuations. This will help maintain a reasonable number of new starts in 1983. While these cuts may be absorbed in the short-run, as a continued policy basis they would inevitably mean decreased productivity from these awards in the acquisition and application of new knowledge.

The 1983 budget as presented will alert the grantee community that it is time to take a careful look at what constitutes indirect costs. The government carefully reviews the need as well as the financial aspects of direct costs. It is appropriate that the basis for the formulation of indirect costs be reviewed. However, since these are real costs faced by grantee institutions for which they will not receive reimbursement, the impact of this cap upon research programs of the grantee scientists is unclear.

Question: What will it do to the ability of grant recipients to produce good science and good researchers?

Answer: A reduction of funding, particularly a reduction in committed funding, is an impediment to the production of good science. The allocation of funds initially is on the basis of careful review of proposed direct costs. A one time cut of 3 to 4% may not be devastating, but we must be very careful that a procedure which is necessary at one point in time because of overall economic circumstances does not become a recurrent policy.

The training of researchers requires not only institutional excellence but also the availability of resources to meet the cost of the training. While limitation of such costs is inevitably necessary, it must be recognized that there is a consequence in terms of a less satisfactory training experience which probably results in a less productive investigator. In view of the substantial funds that will be expended during the professional career of an investigator, excellence in training is a very sound investment.

IMPACT OF CONTINUING RESOLUTION

Question: What has been the impact of the 1982 Continuing Resolution which imposed the lower of the House or the Senate figures and a 4% reduction beyond that?

Answer: For NHLBI the House Allowance was about $1.9 million below the Senate and the 4% reduction represents an additional reduction of more than $23.4 million. This fiscal austerity necessitated by the overall economic climate has had an impact throughout the extramural and intramural programs of the Institute. The impact of 3 to 5% cuts in the various categories of programs have been discussed immediately above. An additional facet of the Continuing

Resolution is its expiration on March 31, 1982 and the uncertainty about the final actions for the balance of the fiscal year.

BUDGET

Question: How will the proposed budget affect your program for the coming year?

Answer: The overwhelming fraction of the budget will go for payment of preexisting commitments; this is true even after the 4% cut in each of the line items and paying overhead at 90% of the standard levels. Of the uncommitted funds, the overwhelming fraction will go towards funding competing renewal and new research grants to a level of 545 awards, allowing a 25% funding rate among the approved research grants.

There would be no funds for new Institute initiatives designed to capitalize upon research development or the initiation of clinical trials to validate promising research findings.

Nearly 64% of the Institute's extramural research funds--$310.9 million--will go towards paying 2,225 research project grants. Of the $310.9 million, $73.7 million are available for 545 competing awards. This compares with an estimated 750 in 1982 and an average of 810 in the three years 1977 through 1979.

The budget allows a small dollar increase for research centers. This does not represent the initiation of any new centers, but rather the costs that will be incurred despite the 4% reduction in commitment. These centers include Specialized Centers of Research in Arteriosclerosis, Hypertension, Ischemic Heart Disease, in Chronic Airways Disease, Pulmonary Vascular Diseases, Fibrotic and Immunolic Interstitial Diseases, Pediatric Pulmonary Diseases, and Adult Respiratory Failure, in Thrombosis, in Comprehensive Sickle Cell Centers, and National Research and Demonstration Centers.

We foresee a small increase in the Research Career Program awards to allow a continuation of new awards in important programs such as in the Preventive Cardiology Academic Awards and in the Clinical Investigator Awards. In the aggregate, there is a decrease in our "other" research category.

The training line is of great importance. We will allocate resources in 1983 to support the number of full-time equivalent trainees at 1,374. This compares to 1,550 in 1982 and 1,634 in 1981. These numbers reflect the increased cost of training and of maintaining viability in the Institute's first priority, the investigator-initiated grant base.

The Institute's research and development contracts will number an estimated 180 in 1983 with a small increase for increased research costs and inflation. This compares with an estimated 209 in 1982. New clinical trials--new initiatives--cannot be undertaken. Important trials ready for validation include objective assessment of the possible role of thrombolytic agents in the treatment of acute myocardial infarction, a procedure rapidly spreading without real validation; testing the possible efficacy of Beta-blocker drugs, now shown effective in preventing recurrent heart attack and death, in preventing a first heart attack and death; assessing the uses and long-term benefits of the widely practiced percutaneous transluminal coronary angioplasty (PTCA); assessment of the possible use of platelet active drugs in preventing recurrent heart attack and sudden death; and assessment of techniques for detecting and quantifying pulmonary embolism.

Question: Where will you place your priorities?

Answer: Looking at program substance, our highest priority is the continued acquisition of knowledge about fundamental biological and disease processes relevent to the cardiovascular system, lung, and blood, and the early clinical investigative research therewith. An integral part of this process is insuring that there continues to be at least some continuity in the flow of highly trained research manpower into the research pool. The demonstration and education activities, particularly in prevention, are of paramount importance. Despite the very tight financial circumstances in which we find ourselves, we will be undertaking further activities therein, as well as strengthening our health education programs, particularly in relation to smoking and nutrition. Of necessity, this results in a deemphasis upon the targeted activities, including particularly clinical trials.

These priorities are consistent with trends over the past several years. Thus, between FY 75 and FY 82, the fraction of extramural funds going to research project grants has increased from 44% to 63%.

The fraction of extramural resources for our training programs during these years has remained fairly constant in the range of approximately 6-1/2%. The fraction going towards Institute-initiated grant programs --predominantly the centers-- has also remained essentially constant in the range of 16-1/2%.

However Institute-initiated research and development contracts, which represent predominantly clinical trials, have declined progressively from 29% to 12% of the extramural program resources during this period. This is in part a reflection of the fact that we have started no full scale Institute-initiated clinical trial since FY 78.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: The National Heart, Lung, and Blood Institute has received many new legislative mandates over the past ten years with and since the enactment of the National Heart, Blood Vessel, Lung, and Blood Act of 1972. Concommitant with these new mandates, there have been new research opportunitites, as well as changing perceptions of national health care needs. Institute programs have broadened not only in scientific scope, but also in emphasis upon clinical validation and clinical trials of new treatment methods holding promise, as well as the development of substantial demonstration and control efforts.

In the early and mid 70's we were able to mount several substantial and very important clinical trials; a number of these have now come to fruition, and are discussed elsewhere in the testimony. We also established the National High Blood Pressure Education Program which has undoubtedly been an important contributor in much better recognition and control of hypertension--it is estimated that at the outset of the program no more than 16% of hypertensives were under adequate control, whereas probably 50% are now controlled--and in the substantial decrease of mortality attributed to diseases for which hypertension is the important causative factor. Thus, we have the benefit of about a 5% per year decrease in the age-corrected mortality from stroke and about 3% per year decrease in coronary heart disease mortality.

In the current austere climate it has not been possible for us to initiate on a definitive scale any clinical trial since FY 78, and we do not see this possibility in FY 83.

On the other hand we are maximizing our efforts in prevention and education within our resources. Thus, we are beginning to mount a more forceful program in the areas of smoking and nutrition. The smoking facts are rather conclusive at this time. However, the nutrition message, it is important to note, is at this time less simple and we are still awaiting the results of several major clinical trials and further understanding of other factors for a full fledged nutrition education program.

The spectrum of our responsibilities ranges from the acquisition of basic knowledge through validation of promising clinical findings to the translation of validated knowledge to the public.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: The Institute has taken a number of steps which we felt most feasible and least damaging to program. Thus we have been careful in trying to cull out from our publications those which, if missing, will have the least adverse effect. In staff travel we have combined more and more site visits into a single itinerary but we find less availability of other site visitors, not government employees, who must also be participants at such site visits. We have made major attempts to decrease our postal and shipping expenses. We have always tried to run the National Heart, Lung, and Blood Institute as economically and cost effectively as possible.

Question: What are your most important administrative concerns--and what are your least important concerns?

Answer: Following are our administrative concerns in descending order of importance.

Our inability to attract and then hire staff with the expertise needed to handle the rapid shifting technologies of our programs is a major impairment to our programs. The personnel freeze makes it impossible to recruit in an effective manner because we cannot make committments without complicated appeals and extensive delays. During this period, highly desirable professional people accept positions elsewhere.

Related to the above constraint are the difficulties in appointing part-time and temporary consultants with the expertise needed. Program costs continue, but effectiveness is impaired. Our ceilings for such services are being steadily reduced and are near the point of being so restrictive we will be unable to obtain the services needed to provide objective outside review of our programs.

Our limitations on travel funds restrict our ability to adequately monitor our grants and contracts and provide for the scientific exchange needed by intramural scientists to remain abreast of the latest scientific advances.

The long-term pay cap on senior executives has resulted in a steady drain of senior talent and restricted our ability to replace our losses. The recent pay increase only minimally improves this state of affairs as we remain non-competitive with universities and industry for the best talent.

The use of contract airlines often results in a serious drain on staff time. The inability to schedule flights which best suit the individual staff member's schedule means there are extra hours of waiting to return from trips, longer flight times, often increased costs compared to special discount fares, plus extra clerical staff time to make the arrangements and deal with staff who find the travel restrictions illogical and often costly in time and money.

Question: What criteria do you use for determining your administrative priorities?

Answer: Our goals and therefore our priorities are to provide the atmosphere and support resources to maintain a creative and productive program, both in our intramural and extramural programs. Another is to responsibly administer and monitor our grants and contracts programs. Therefore, those matters impinging on the above determine our top priorities such as recruitment of the most highly qualified staff to run our programs and their continued development; careful budget considerations to get the most from our dollars; and the careful attention to the mandates, restrictions, and priorities given us by the Congress and the Department.

In summary, our prime responsibility is the development and maintenance of a National Heart, Lung, and Blood Institute research program which results in the maintenance of health and the relief of suffering. Thus, our first question is always how will this effect our program. We try to maintain a long-term view and maintain long-term goals in the face of the need to achieve immediate accomplishments and economies. It is the delicate trade off between the competing priorities of available resources and needs--both long term and immediate--that we seek to balance carefully.

ARTIFICIAL HEART

Question: Early in 1981, a surgeon in Texas used an artificial heart in a patient for a brief period while the patient was waiting for a heart transplant to take place. While the artificial heart was only in the patient for about 24 hours, a great deal of press coverage focused on the fact that the device had not yet been fully approved for use by FDA. The patient was, however, kept alive successfully as a result of the procedure. Is the artificial heart advanced enough at this time for use in life-threatening situations?

Answer: Devices which can be inserted into the chest to physically and functionally replace the heart have been developed in several laboratories. There are varying degrees of experience in animals with such artificial hearts. There is no question that they can maintain the circulation. The critical question is whether there are clinical circumstances in which such a pump can be of benefit.

The pumps developed to date are fundamentally for short-term use. They have to be connected to an external source of energy and controls for their function. The use of such a pump in a patient who is essentially dead and who would require and would get a cardiac transplant is an arguable basis for the use of such an artificial heart. Difficult judgments remain in identifying a person who is so close to dead that such a drastic interim procedure is necessary and avoiding the person who is so far dead that irreversible damage has taken place in other organs of the body, particularly the brain.

There is now considerable experience with ventricular assist devices which are often referred to as "artificial hearts." These are pumps which are added to the pumping system of the heart and may replace the functioning of the ventricle but do not involve the removal of the heart. For example, in a recent report, published in the New England Journal of Medicine, of 8 most recent patients, in whom the ventricular assist device was used--patients who were moribund because, despite a technically successful open heart procedure, they could not be taken off the heart-lung machine--4 patients were long-term survivors. This ventricular assist device, or auxiliary pump was kept outside the body and connected to the heart and arterial system by tubing. After several days the external apparatus was removed and the survivors were left with their original hearts.

The discussion of ventricular assist devices is presented for clarification and to indicate where the greater fraction of mechanical circulatory support research is now ongoing. It is also important to note that the major thrust of "artificial heart" research at this time is in the direction of long-term fully implantable ventricular assist devices which will allow its recipient at least two years (perhaps five years) of good quality life with close to normal everyday activities. It will require recharging of its energy source one, two, or perhaps three times a day, but an otherwise relatively normal existence.

Question: When can we anticipate that such a device will be approved for use?

Answer: The Food and Drug Administration has given approval for investigational use of a short-term artificial heart to the University of Utah within the last several months. To the best of our knowledge, the device has not been used, presumably because the clinical circumstances for its use have apparently not arisen.

CORONARY BYPASS SURGERY

Question: We understand that coronary bypass surgery constitutes one percent of the total cost of national health care. Is it cost-effective?

Answer: As discussed during the testimony, coronary bypass surgery is undertaken in different patients with different goals. In some it is with the expectation of improving life expectancy, and as noted, the evidence for improved life expectancy is firm in the small group of patients with left main coronary disease but less firm in other groups. For example, in patients with significant disease of all three major coronary arteries there are studies which show improved life expectancies but the judgment of an expert consultant group in the consensus document already submitted for the record indicates that it would be desirable to confirm these results from further studies. The evidence for improved life expectancy in patients with two-vessel disease is tenuous. The second and perhaps more common use of the surgical procedure is the relief of symptoms of angina pectoris and the achievement of an improved quality of life. The procedure is effective in relieving angina in the vast majority of patients and an improved quality of life is generally achieved, though such economic indices as return to work are surprisingly little influenced. However, the return to work issue is importantly clouded by social and economic issues such as Workmen's Compensation, period of prior time away from work, the nature of the work, etc.

From the foregoing it is clear that coronary bypass surgery is performed for many different reasons, in patients with widely differing degrees of prognosis for life expectancy and with quite varied quality of life at the outset. Thus, while the cost may be in a range which is not terribly broad, the effectiveness varies tremendously in the sense of how much is gained, with what certainty and compared to what alternative options of management. Certainly for patients in whom an improved life expectancy is clearly demonstrated, and in patients whose lifestyles are seriously compromised despite intensive and carefully individualized efforts at medical management and lifestyle improvement, it must be considered cost effective by the standards that society ordinarily uses.

We are seeking through our ongoing studies, including the Coronary Artery Surgery Study, more precise assessment of the true long-term effects and benefits of the procedure and its alternatives.

Question: Are there better alternatives to such surgery?

Answer: From the prior response it is clear that one has to speak of specific subgroups of patients and cannot discuss the procedure in the aggregate.

For most patients with coronary artery disease, the first line of therapy includes optimization of lifesytle, and pharmacological therapy, as well as advice and reassurance of what symptoms mean and what they don't mean. It is helping the patient to live optimally with his or her disease. Indeed, one of the already important findings from a broad spectrum of research is that concurrent with the dramatically improved results of coronary bypass surgery over the past 12 or so years there has been a dramatic improvement in the effectiveness of the medical management of patients with coronary artery disease.

An exciting development has taken place within the past three years-percutaneous transluminal angioplasty (PTCA). In this procedure, certain narrowed coronary arteries can be dilated by means of a special cardiac catherization procedure and the surgery can be obviated. The Institute has developed a registry in which we now have data from approximately 3,000 patients. From this it seems that the procedure has been refined to the point that its immediate results are effective in 60% or more of the patients in whom the procedure is undertaken, and bypass surgery is not needed. In a small percentage complications dictate emergency surgery.

It must be noted that to date PTCA has been used predominantly in patients with only one of their three major coronary arteries significantly diseased, yet with symptoms sufficient to dictate surgery were it not for PTCA. This group of patients is probably no more than 5% of patients who now undergo coronary bypass surgery. One area of research is better understanding of the outcome of the procedure when it is used in patients with lesions in more than just one vessel. A critically important issue is obtaining reliable data about the long-term course of patients who undergo PTCA--how they fare three years, five years and longer after the procedure.

Continued improvement in completely medical therapies for coronary artery disease is also an important topic of research, and promising avenues include the newly available class of drugs known as calcium channel blockers.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Question: Given the rapid rate of increase of Chronic Obstructive Pulmonary Disease, what opportunities do you see for NHLBI to help reverse this troubling trend?

Answer: Mortality from Chronic Obstructive Pulmonary Disease (COPD) is indeed on the increase. In 1980, over 55,000 Americans died from this illness which makes it the fifth major cause of death in the United States. The emphasis of research supported through the NHLBI has been to identify risk factors, determine natural history, develop methods for early detection and elucidate the pathogenesis of the disease process. Since important advances can be reported in all areas, the Institute is now looking toward the time that screening programs may be established to identify individuals at risk and prevent the disease process before it becomes irreversible.

Research investigations from several laboratories have led to the current concept for the pathogenesis of destructive lung disease which suggests that the maintenance of normal alveolar structure and function is dependent on the existence of a homeostatic balance between proteolytic enzymes called elastases and their inhibitors within the lower respiratory tract. This protease-antiprotease scheme for the pathogenesis of this disease holds that the characteristic destructive lesion results from an excess of elastase activity and/or a deficit of anti-elastase activity within the lower respiratory tract. This process appears to be identical in both the acquired form of destructive lung disease that is associated with cigarette smoking (the major risk factor for COPD) and the hereditary form of destructive lung disease associated with alpha$_1$antitrypsin deficiency.

Concepts developed by pulmonary physiologists have lead to a wealth of information on the functional characteristics of the respiratory system. From this research a working hypothesis has been set forth, that in the transition from health to the established morbidity of COPD, there is a temporal progression of structural abnormalities that can be measured by tests of lung function. These investigations have lead to an understanding of the concepts of functional abnormalities that represent important manifestations of the disease. Results from this research on lung structure and function lead us to be optimistic that biochemical tests and pulmonary function measurements may someday be used to identify the individual who is developing COPD at a time when the disease process is still reversible.

ASTHMA

Question: Asthma is the most common chronic respiratory disease in children and also a severe problem in adults. What more can NHLBI do to relieve this problem?

Answer: More than nine million Americans suffer from asthma, an important medical cause of restricted activity. The substantial adverse effect of this disease on the quality of life justifies placing it high on the list of priorities for medical research. It is a major cause of physician visits, an important reason for hospitalization and, especially in younger age groups, the cause of many person-hours lost from the workplace or classroom.

Despite major advances in pharmacological treatment over the last ten years, asthma continues to be a considerable problem to clinicians and its management is still far from straightforward. Much remains to be learned about the natural history of the disease and the influence of treatment upon it. If progress is to be made in the prevention of asthma, rather than in merely suppressing it or relieving its symptoms, a better understanding of its etiology is essential. Although studies of the familial incidence of asthma have made it clear that there is a strong genetic basis for this disease, it is still impossible to identify subjects who are predisposed to developing the disease. A major goal of the NHLBI program is to understand the pathogenesis of the disease process. For example, one of the characteristic features of asthma is extreme sensitivity of the airways to physical, chemical, pharmacologic and emotional stimuli. Various theories have been proposed implicating abnormalities in the autonomic regulation of airway smooth muscle in the pathogenesis of asthma. Another important goal is to determine whether or not asthma in early life predisposes the individual to the development of chronic obstructive pulmonary disease.

The NHLBI has taken an active role in developing education programs for pediatric patients with asthma. Investigators have developed and compared various methods for teaching self-management to the asthmatic child and his or her family. These education programs have been shown to have a significant impact on the asthma condition including reduction in asthma attacks, hospitalizations, and use of health care resources (such as the emergency room). The effectiveness of these patient education programs must now be demonstrated in additional populations and the results translated from the health education community to the physicians who treat asthmatic children. Similar programs for the adult asthmatic need to be developed and tested.

ENVIRONMENTAL AND OCCUPATIONAL HEALTH RESEARCH

Question: There is obviously a critical and growing need for environmental and occupational health research. What role do you see for NHLBI in meeting this need?

Answer: Because the respiratory tract has intimate, continuous exposure to environmental air and because inhalants in the environment including the workplace may cause respiratory health effects, the NHLBI has among its mandates support of research related to environmental and occupational lung disease.

A few years ago, the NHLBI published a major task force report entitled "Epidemiology of Respiratory Disease." Both environmental agents and occupational agents received major attention by the task force. Recommendations for research directions in both areas were made which are anticipated to stimulate research grant applications from the respiratory community. Every effort will be made to support as many of the research grants as possible. Examples of the types of projects now supported by the Institute include research on effects of air pollutants such as oxides of nitrogen and ozone on the respiratory tract, how pollutants alter the normal function of lung cells, how these changes can cause illness and exacerbate existing disease, and how the lung handles foreign substances. The Institute supports three Specialized Centers of Research in Fibrotic and Immunologic Lung Disease which have as their objectives understanding the pathogenetic processes that lead to pulmonary fibrosis, one of the respiratory conditions that is triggered by such agents as mineral dusts (e.g. coal, silica, asbestos, beryllium). Exposure to organic dusts, such as cotton and grain, produce allergic alveolitis and hypersensitivity pneumonitis, lung diseases also under study by NHLBI researchers.

CYSTIC FIBROSIS

Question: Cystic Fibrosis is the most common genetic disease among caucasian children. What NHLBI activities are addressed to this problem?

Answer: Cystic fibrosis is an inherited disease presumably transmitted in an autosomal recessive manner. No biochemical basis for the disease has yet been defined. Although there is wide variation in clinical symptoms and organ involvement, in its most common manifestation, cystic fibrosis seems to affect primarily the mucus-secreting glands and cells of the body. Large amounts of thick secretions are produced resulting in ductal obstruction and impairment of function of various organs with two main target organs, the lung and the gastrointestinal tract. In the lung, airway obstruction and secondary infection represents the major clinical problem in the disease. Although a considerable amount of information has been generated concerning all aspects of cystic fibrosis, results that have an immediate application to early detection, prevention or treatment of this disease have been disappointing. On the positive side, the most recent survival studies indicate that 50 percent of patients now survive to age 20; data available 10 years ago indicated a median survival of approximately 10 years.

The NHLBI supports research related to the structure of the mucus glycoproteins in cystic fibrosis compared to normal in an attempt to establish the mechanisms by which mucous secretions are regulated. Basic studies of host defense mechanisms, especially as they relate to the determinants of pseudomonas colonization in the lungs of the cystic fibrosis patient are also underway. However, the major breakthrough in cystic fibrosis research will only come when tests for prenatal diagnosis are available so that preventive programs can be initiated. Hopefully, the techniques of molecular biology may someday be used to identify the presence of the abnormal cystic fibrosis gene. Development of this approach may facilitate programs of genetic counseling.

ADULT RESPIRATORY DISTRESS SYNDROME

Question: The impact of Adult Respiratory Distress Syndrome on mostly young, previously healthy individuals is of concern. Will you describe the problem we face and what NHLBI is doing to overcome it?

Answer: The Adult Respiratory Distress Syndrome (ARDS) is characterized clinically by diffuse pulmonary infiltration, marked respiratory distress, impaired lung compliance, and hypoxemia that responds poorly to ventilatory assistance. ARDS affects approximately 150,000 adults each year, a number likely to increase as the means for speedy evacuation and resusitation of trauma victims improves. The mortality rate from ARDS is about 50 percent; many of the victims are often young, previously healthy individuals, involved in a traumatic accident.

Initial research efforts in this area focused on development of methods for ventilatory assistance and oxygenation because of the belief that lungs of ARDS victims could recover if death did not interrupt the healing process. Extra-corporeal membrane oxygenation (ECMO), the ultimate of these life-support strategies, became available in the early 1970's affording the possibility of long-term support of lung function by artificial means. However, by the mid 1970's, it became clear that ECMO was no more effective in salvaging patients with severe ARDS than less expensive, conventional methods. Thus, the Institute modified its program goals and initiated a program designed to identify the nature of the lung injury that leads to the onset of respiratory failure. In 1978, three Specialized Centers of Research in Adult Respiratory Failure were initiated. The results from this program have been extremely encouraging. Promising new techniques for early detection of ARDS have been reported, such as detecting lung endothelial damage and presence of mediators in the circulation which can cause this injury. The multidisciplinary approach has helped to solidify certain facts about the basic pathophysiologic changes that occur with this syndrome. Much work remains to be done, however, to reduce mortality from this illness. This will require interactions of cell biologists, biochemists, immunologists, and physiologists with pulmonary physicians familiar with the care and treatment of the patient in respiratory failure. The Institute has announced another competition for Specialized Centers of Research in Adult Respiratory Failure in an attempt to stimulate interaction between multidisciplinary teams to explore new research initiatives in acute lung injury and repair mechanisms.

EMPHYSEMA

Question: What progress are you making in screening for and curing emphysema?

Answer: Nearly three million Americans suffer from emphysema, a chronic, debilitating disease of the airways for which there is no cure. In most people, emphysema is caused by cigarette smoking. A small proportion of people with emphysema have a genetic defect that results in a deficiency of a glycoprotein, $alpha_1$antitrypsin. Those individuals who are homozygous for $alpha_1$antitrypsin deficiency can be identified through laboratory tests from blood samples. In fact, tests for $alpha_1$antitrypsin can be made from cord blood samples at birth. These tests are not routinely conducted on newborns because of the relatively low incidence of this genetic trait but can be done if the family has a history of this defect.

Avoidance of cigarette smoking is critically important to individuals who have this genetic deficiency.

Screening for early detection of the acquired form (e.g. associated with cigarette smoking) of emphysema remains a subject of intense interest. Research scientists have provided a wealth of imaginative and ingenious experimentation that has led to an understanding of the pathogenetic processes that lead to destruction of lung tissue resulting in development of emphysema. The question remains whether tests of lung functon can be used for detection of emphysema at a stage before the disease process becomes irreversible. The NHLBI has initiated steps to explore the scientific information that is available to establish whether existing technology for pulmonary function evaluation can be used as a means of preventing the serious consequences of chronic airflow limitation in a large number of subjects. Participants from voluntary health organizations and the federal government will work together to develop steps that must be taken to meet this challenge.

Question: How serious is the emphysema problem nationwide?

Answer: Diseases characterized by severe and persistent airways obstruction have become increasingly important causes of disability and death in the United States. The term chronic obstructive pulmonary disease (COPD) is a widely used term that combines both chronic bronchitis and emphysema, disorders associated with irreversible airways obstruction. In 1979, it was estimated that 9.6 million Americans suffered from COPD, 2.1 million with emphysema, and 7.5 million with chronic bronchitis. Chronic respiratory diseases account for approximately ten percent of disability benefits granted by the United States Social Security System and for lost hours of work estimated to be as high as 250 million man-hours annually. Disabling chronic airways obstructive disorders are reported as much as 9 to 10 times more frequently in men than in women. However, the frequency of these diseases in women appears to be increasing, presumably a result of the increasing number of women who smoke cigarettes.

BLOOD RESEARCH

Question: Last year, your Institute provided the committee with a summary of accomplishments in blood research over the past ten years. Which of your recent advances in blood research are now available to practicing physicians for use in patient care?

Answer: Numerous advances in both blood diseases and blood resources have been translated into patient care. Most significant among these in blood diseases are:

1. Treatment of hemophilia using factor VIII concentrates.
2. Treatment of hemophiliacs who have inhibitors (antibodies) to factor VIII with prothrombin complex concentrates.
3. Prevention of deep vein thrombosis using anticoagulants and anti-platelet agents in surgical and other high-risk patient groups.
4. Treatment of venous thrombosis and pulmonary embolism with thrombolytic (clot dissolving) agents.

5. Detection of venous thrombosis by non-invasive methods.
6. Treatment of iron overload in thalassemia with iron-chelating agents (Desferal).
7. Diagnosis and treatment of eye complications in sickle cell disease patients.
8. Diagnosis of sickle cell disease in the newborn.

Among the significant advances in blood resources have been:

1. Better management of the nation's blood resource.
2. Platelet therapy in cancer patients.
3. Interferon production and clinical use.
4. Granulocyte transfusions for carefully selected patients.
5. New and improved plasma derivatives.
6. Screening donated blood to prevent transfusiontransmitted hepatitis.
7. New and improved products for treatment of hemophilia.
8. Artificial substitutes for red blood cells.
9. Prevention of type B hepatitis with a newly licensed vaccine.
10. Treatment of chronic diseases by the selective removal of blood components (therapeutic apheresis).

Question: What impact are they having?

Answer: The advances in the prevention, diagnosis, and treatment of blood diseases are having the following impact:

1. The availability of freeze-dried factor VIII concentrates has made home care possible for many hemophiliacs. While these patients tend to use more factor VIII per year than those who are not on home care, they require fewer visits to the hospital or clinic, have an improved quality of life, and lose fewer days at work or school.
2. Hemophiliacs with inhibitors to factor VIII present a difficult management problem when they have major bleeding episodes or require surgery. Some can be treated with large doses of factor VIII, enough to overcome the circulating inhibitors. Others, however, cannot be treated in this manner. Availability of prothrombin complex concentrates (PCC), which apparently bypass the factor VIII-requiring step in clotting, allows partially effective treatment of patients. Research is underway to develop more effective products, but until such become available, the use of PCC is the regimen of choice for the treatment of joint

bleeds or in other instances in which effective hemostasis is required.

3. Application of preventive methods for deep vein thrombosis in several high risk groups of patients is now part of routine clinical practice. Although statistics are not yet available, the demonstrated efficacy of these methods applied to the large number of patients involved would lead to significant reduction in mortality and morbidity as well as health care costs. Different methods, including low-dose heparin, aspirin, and other antiplatelet drugs, and intermittent pneumatic compression, have been shown to be effective in different groups, depending to some degree on the probable mechanism of clotting.

4. Studies supported by the NHLBI provided the evidence for clinical efficacy and safety of thrombolytic agents in the treatment of pulmonary embolism, which subsequently led to FDA licensure of these drugs. They are now available to practicing physicians and are being used more and more frequently for both pulmonary embolism and deep vein thrombosis. Dissemination of the results of a consensus development conference sponsored by the Institute in 1980 was a major factor in increased recognition and use of these drugs. One of the most exciting recent developments in cardiology has been the apparent effectiveness of thrombolytic agents in dissolving the clot which causes about 80 percent of acute myocardial infarctions. However, this use is still considered experimental, and there are no firm data upon which to assess overall effectiveness in comparison to other treatment modalities.

5. Venography has long been considered the "gold standard" in the diagnosis of venous thrombosis. However, it is an invasive procedure requiring the injection of contrast material before x-rays are taken, and the frequency of its use in following progression or regression of the thrombotic process is limited. Newer methods now in common use, including ^{125}I-fibrinogen scanning, doppler ultrasound, and impedence plethysmography, are safer for the patient and can be done repeatedly to monitor therapy.

6. Hypertransfusion of red blood cells has now been adopted as standard medical practice for the treatment of the severe anemia associated with Cooley's anemia. In order to reduce the toxic iron buildup resulting from the repeated transfusions, the subcutaneous infusion of Desferal has been introduced as standard part of therapy. These procedures have improved the quality of life, and while long-term efficacy remains to be demonstrated, the results at this time look very promising.

7. Advances in clinical research have documented the existence of eye complications which may lead to blindness in patients with sickle cell disease. A standardized classification of the evolution of sickle cell retinopathy into sequential stages is now available to the

practicing physician. The clinician is aware of these potential problems in sickle cell patients and has an increased "index of suspicion" leading to more thorough ocular examinations, earlier diagnosis of complications, and appropriate referrals.

8. The development of new, simple electrophoretic techniques have now made the early diagnosis of sickle cell disease possible in newborns from cord blood samples. Hemoglobin electrophoresis with cellulose acetate and citrate agar provides accurate diagnoses even in the presence of small amounts of sickle hemoglobin. This identification of patients in early infancy permits immediate education and counseling of the parents about the risks of sepsis, which is the most devastating complication contributing to mortality and morbidity in this age group. The physician who is knowledgeable of this diagnosis is more alert to problems and can respond more aggressively to potentially life threatening infections. The entry of the infant into the health care delivery system, before developing complications, has increased the potential for reducing early morbidity and mortality.

The advances in collection, preparation, and use of blood resources are having the following impact:

1. The management of the national blood resource has improved significantly with the increasing use of blood components. This improvement can be seen in the changing pattern of red blood cell usage. During 1971, approximately 21 percent of all red blood cell transfusions were administered as components and the remainder were transfused as whole blood. In contrast, during the year 1979, approximately 77 percent of all red blood cell transfusions were transfused as components and only 23 percent as whole blood. This reduces the chances for adverse reactions and expands the number of patients who may benefit from the available blood supply.

   In 1977, the Food and Drug Administration (FDA) licensed the anticoagulant preservative solution citrate-phosphate-detroxe (CPD) supplemented with adenine. Erythrocytes stored in this solution maintain higher adenosine triphosphate concentration than those stored in CPD alone, thus prolonging the storage period from 21 to 35 days. This procedure of blood preservation has been adopted by many states and constitutes an important step in improving red blood cell preservation. These changes have resulted in increased availability of red cells and whole blood for use by practicing physicians in transfusion therapy.

2. During the last decade, the technology of separating the platelets from whole blood was developed and this method became a routine procedure. Thus, platelets became available to an ever larger segment of the patient population. In 1971, about 400,000 units of random platelet concentrates were transfused, whereas the corresponding number in 1979 was 2.2 million.

Studies involving short-term preservation of random platelet concentrates helped to define the maximum storage period at 22 degrees centigrade as 3 days. This storage technique was approved by the FDA and adopted into general blood banking practice. Ability to store platelets resulted in better management of platelet inventories nationwide. More recent advances have extended the maximum storage period to 5 days.

Single-donor apheresis platelets also became available to many patients due to the development of improved blood cell separators. Transfusing single-donor platelets is preferable to giving several units of random platelets because the risk of posttransfusion hepatitis is lower and because sufficient quantities of HLA-matched compatible platelets can be given to immunized patients.

These advances have made more platelets available, thus enabling physicians to treat many forms of cancer more aggressively.

3. Human leukocytes provided by blood collection agencies have been used as a source material for large-scale interferon production. Over 95 percent of the interferon used in human clinical trials has been human leukocyte interferon. A more potent acting interferon, immune interferon, is also obtained from properly stimulated lymphocytes. Large-scale production of interferon from human peripheral lymphocytes in Finland made possible limited clinical studies to determine the therapeutic effectiveness of interferon in certain viral diseases and malignancies. Use of interferon appears beneficial in herpes keratitis, in some respiratory infections, herpes zoster, hepatitis, osteosarcoma, and certain malignant diseases.

4. During the last decade the effectiveness of granulocyte transfusions was evaluated in many clinical studies. They were shown to be effective as an adjunct to antibiotic therapy in patients with neutropenia and documented gram-negative septicemia. Septic patients with functionally abnormal granulocytes and patients with progressive local infections appeared also to benefit from such therapy.

5. Since 1972, improved technology has been developed for production of plasma proteins already used therapeutically and for the isolation of a host of new proteins. New mild, nondenaturing precipitants have been used for the isolation of plasma proteins. These include polyethylene glycol for albumin, factor VIII, C-1-inhibitor, and antithrombin III; and polyelectrolytes for the preparation of factor VIII. Mild denaturants such as dithiothreitol have been used for the preparation of intravenous immune globulin and alpha-1-proteinase inhibitor (alpha-1-antitrypsin). The use of ultrafiltration techniques to concentrate and desalt plasma fractions has also been developed since 1972. In fact, this process is now being routinely used in the production of both Immune Serum Globulin and Normal Serum

Albumin. A second method for protein concentration, thin film evaporation, is also being utilized in the manufacture of albumin.

In the area of immune globulins, the use of RH_0(D) Immune Globulin, whose primary indication is prevention of postpartum sensitization, has been extended to include administration to Rh-negative women after miscarriage, abortion, or amniocentesis.

New immune globulin products that have become available during the last decade include two types of preparations. One type includes specific immune globulins for intramuscular use, viz., Rabies Immune Globulin (commercialized in 1974), Hepatitis B Immune Globulin (1977), and Varicella-Zoster Immune Globulin (1980).

The year 1981 witnessed the introduction of Immune Globulin, Intravenous, the only human immunoglobulin product for intravenous use that is currently on the American market. Whereas the indication for its use, namely, maintenance of immunodeficient patients, is the same as one of those for Immune Serum Globulin, the process by which it is manufactured is strikingly different. The advantages of intravenously administrable immune globulin (compared with the conventional product, which is given intramuscularly) are the greater comfort for the patient, the rapid attainment of high levels of antibodies in the circulation, and the fact that larger doses can be administered. The latter advantage is particularly significant when intensive therapy is required or when the patient's musculature is small or damaged.

6. Of major importance for public health was the introduction, in 1972, of testing for the hepatitis B surface antigen (HBsAg). This testing, which is now performed by methods with considerably higher sensitivity, is applied to all blood or plasma, regardless of whether it is intended for transfusion or fractionation. Furthermore, plasma derivatives are now devoid of detectable HBsAg.

   A number of prospective studies of transfused patients have documented an 85 to 90 percent decrease in the incidence of hepatitis following the transfusion of blood since the introduction of sensitive radioimmunoassay tests to detect HBsAg. Nationwide there has been a progressive decrease in cases of posttransfusion hepatitis that has paralleled the use of these tests with increasing sensitivity to detect HBsAg.

7. The use of purified Antihemophilic Factor, which can be stored at room temperature or under ordinary refrigeration, in the treatment of hemophilia has increased greatly while the use of cryoprecipitate, which must be frozen, has diminished.

   The use of cryoprecipitated antihemophilic factor for replacement of fibrinogen in those few patients for whom it is necessary and the use of factor IX complex for patients with inhibitors (antibodies to factor VIII) are examples of new indications for existing coagulation products. The use of factor IX complex for the treatment of patients with factor VIII inhibitors is more innovative. It is estimated that 10 to 15 percent of patients with classic hemophilia A will develop an antibody to factor VIII. In such patients, therapy for major bleeding episodes may be effective only if the factor VIII is infused in massive amounts, or if the inhibitor level in the plasma is decreased by plasmapheresis or plasma exchange before infusion of factor VIII. Despite these procedures, however, management of the disease constitutes a serious problem when the inhibitor level of antibody precludes the possibility of successful therapy with AHF concentrates. In these situations, factor IX complex has been used with beneficial effects. The results of a multicenter therapeutic trial (1980) unequivocally established the value of factor IX complex in the treatment of hemarthrosis in hemophilia A patients with inhibitor.

A new coagulation product introduced in 1981 is the Anti-Inhibitor Coagulant Complex (AICC). This product is described as being a "controlled, activated prothrombin complex concentrate" (prothrombin complex is a term used by some investigators for factor IX complex). AICC is intended for use only in patients with factor VIII inhibitors who are bleeding or are to undergo surgery. Although there has been no double blind, controlled clinical trial of the product, its effectiveness in stopping bleeding is recognized.

8. In the area of blood substitutes significant progress has been made with perfluorochemical-type preparations. Clinical investigations with perfluorochemical-containing preparations have been carried out in Japan, Europe, and the United States. The product used contains an emulsion of perfluorodecalin and perfluorotripropylamine; the presence of the latter aids in stabilizing emulsions of the former. Hydroxyethylstarch is used to maintain osmotic pressure.

   Worldwide over 400 patients have received the material for a variety of both hemorrhagic and nonhemorrhagic problems. In the United States a dozen patients who, for religious reasons could not accept blood transfusions, have been treated with blood substitutes.

9. Under the sponsorship of the NHLBI, the first major clinical trial of a new vaccine developed by Merck, Sharp and Dohme to prevent type B hepatitis has been completed. The vaccine consists of highly purified, formalin-inactivated virus subunits derived from the plasma of chronic carriers of type B hepatitis. The vaccine was licensed by the Food and Drug Administration in 1981 and will become available in 1982.

   The vaccine was shown to provide virtually complete protection against the development of type B hepatitis.

After booster shots, 96 percent of those inoculated showed increased antibody response rates through 18 months of followup.

The development of the hepatitis B vaccine and the demonstration that such a vaccine prevents type B hepatitis infection are major advances in the control of this extremely widespread disease.

Although most carriers of hepatitis are asymptomatic, a substantial proportion eventually develop chronic active hepatitis and cirrhosis. There is also overwhelming evidence that the hepatitis B virus is the single most important causative factor of hepatocellular carcinoma. Thus, mass immunization programs may ultimately affect not only the incidence of acute hepatitis B and the pool of chronic carriers, but may also reduce the morbidity and mortality from chronic active hepatitis, cirrhosis, and hepatocellular carcinoma.

10. Therapeutic apheresis is a procedure by which blood is withdrawn from a patient, a specific component is separated from the blood, and the remainder is returned to the patient. Although still an experimental therapy, approximately 16,000 therapeutic apheresis procedures were performed in 365 hospitals and blood centers in 1979. Apheresis was used in the treatment of many different chronic diseases including Goodpasture's syndrome, systemic lupus erythrematosus, glomerulonephritis, multiple sclerosis, and complications of rheumatic diseases.

NATIONAL BLOOD POLICY

Question: Where do we stand in regard to planning for a blood-sharing network to ensure equitable access to blood for patients nationwide?

Answer: Community, regional, and national programs each contribute to equitable access to blood by patients across the United States. About 95 percent of blood for transfusion is collected, processed, and distributed through established community and regional networks of blood centers and hospitals. The other 5 percent of blood needed for transfusion is supplied through long-term contracts between surplus regions and shortage regions and through special requests handled by programs such as the Clearinghouse of the American Association of Blood Banks. Four national organizations (the American Blood Commission, the American Association of Blood Banks, the American Red Cross, and the Council of Community Blood Centers) have agreed on the framework for one nationwide network to more efficiently and equitably meet interregional and special blood needs. The national network will be built on the existing systems.

Question: Would any such plan be privately funded — or would it involve Federal participation?

Answer: The cost of one nationwide network built on existing systems and incorporating principles already agreed upon to ensure equity will be minimal. The nationwide network will be privately supported and no Federal participation is planned.

HYPERTENSION

Question: To what extent does current evidence support the notion that non-drug therapies, such as weight control, salt restriction, and exercise, contribute to the control of high blood pressure?

Answer: In the National Heart, Lung, and Blood Institute published report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, it is noted regarding non-pharmacologic therapy that "Epidemiologic studies show a strong association between blood pressure and body weight, as well as between blood pressure and sodium intake."

A few studies on the effects of dietary intervention suggest that weight reduction or moderate control of sodium intake may lower blood pressure in some patients. The conclusions of these studies require confirmation through larger clinical trials.

In general, weight reduction in obese subjects and sodium control in all patients should be considered adjunctive to the management of hypertension.

Dietary management is a reasonable initial approach in young patients with uncomplicated mild hypertension and no additional cardiovascular risk factors. To be successful in the long run, extended nutritional counseling may be necessary. If nondrug treatment reduces blood pressure and maintains it at normal levels, it may be considered definitive therapy. If diet proves ineffective in normalizing blood pressure after an adequate trial, drug therapy should be considered in addition. It is not known at this time what proportion of all hypertensives are salt-sensitive.

Studies on behavioral methods of hypertension management, such as biofeedback, psychotherapy, and relaxation, suggest that small blood pressure reductions are possible in some patients. These methods are still experimental and not routinely recommended. Their potential use in borderline or very mild hypertension is promising.

Information regarding the beneficial effects of exercise in hypertension is interrelated with weight modification effects. Investigators have reported that long-term improvements in exercise and eating habits have yielded sustained weight loss with beneficial effects on blood pressure in persons with mild hypertension.

More limited research on the role of exercise in the control of high blood pressure is being conducted. In one interesting study involving genetically spontaneously hypertensive rats the animals were exercised systematically starting at two weeks of age. By eight weeks of age the animals had lower blood pressure levels than unexercised ones. The report suggests that systematic exercise delays the onset and blunts the magnitude of blood pressure increase in these animals.

Question: To what extent is the Institute researching these alternative approaches?

Answer: The Behavioral Medicine Branch/NHLBI in 1980 issued an announcement in the NIH Guide for Grants and Contracts to encourage clinical research projects dealing with evaluation of combinations of pharmacologic and non-pharmacologic therapies in the treatment of patients with diagnosed essential hypertension and requested investigators to consider applying for regular research grant support in this area. The Institute is currently supporting ten research grants submitted in this area of research.

Within the past year, the Institute has issued a program announcement that was published in the NIH Guide to Grants and Contracts to encourage the submission of applications concerning a broad range of investigations, including basic, physiological, clinical, epidemiological, preventive and therapeutic, regarding the role of sodium and related electrolytes in hypertension.

The primary objective of one intervention study is to ascertain if weight reduction and sodium restriction can be utilized in the control of vascular hypertension with resultant decrease or discontinuance of drug therapy.

The rationale for this study hinges on: 1) the issue of benefit to risk ratio associated with long term drug use to control hypertension; 2) the evidence that overweight and excess salt intake may have hypertensive effects; and 3) the stated need to determine the extent to which drug treated hypertensives may be withdrawn from drug therapy. One working hypothesis is that using diet restriction and weight reduction, normal blood pressure levels can be maintained in mild hypertensives who have been normalized pharmacologically over a protracted period.

A second intervention study in three clinical centers is testing whether sodium restriction plus elevation of potassium intake as one intervention, and weight loss as another intervention reduces substantially the number of patients requiring return to drug therapy after prolonged drug therapy is stopped. Identification of characteristics that may predict whether dietary change can be expected to be of benefit and the extent to which the patients actually do change their diets are being monitored and quantified.

The Institute in September, 1981, began grant support for an investigator initiated five year feasibility study at four clinical centers, a data coordinating center, and a nutrition and education resources center for Phase I of a randomized clinical trial to determine whether hypertension can be prevented by dietary intervention in a population of 18-40 year old men and women with increased risk of developing hypertension. Findings in the feasibility study will be used to determine whether a full-scale Phase II trial to prevent sustained hypertension should be conducted. (Total costs for the six individual grants for the five year period is approximately $10 million. While the costs of proceeding to the full-scale trial if warranted from the results of Phase I have not been formalized, Phase II would involve as many as 6,000 participants and a minimum of 5 years of follow-up.)

Question: What is the result of the clinical trials that the Institute has been conducting on the role of salt and water balance in hypertension?

Answer: The two dietary intervention trials, which include five clinical centers, are proceeding with enthusiasm from participants and staff, as well as investigators. They are continuing to follow the participants with special dietary protocols as proposed, including sodium restriction. Study results are anticipated within the next year. Preliminary results are promising to date.

TRAINING

Question: In last year's hearing you discussed the drop in the number of clinical investigators participating in the Institute's training programs, and listed some of the factors contributing to the decline. These included uncertain levels of training funds and research grant money, as well as low training stepends that are not competitive with other options available to physicians. Where do matters presently stand?

Answer: The factors listed last year are still the main deterrents to clinical investigators participating in the Institute's training programs. However, the NHLBI continues to seek to encourage the clinician to engage in research, and it is particularly important that the MD should be given the opportunity of formal training, since the doctoral education of the physician usually involves very little exposure to research. The number of MDs in receipt of training awards from the NHLBI was at an all-time high in 1972, but fell abruptly, by 20% in 1973. In 1981, following further fluctuations in the 70s, we had managed to regain about the same level as in 1973, principally by the introduction over the past few years of successful new strategies such as the clinical Investigator Awards, the Pulmonary Academic Awards and the Preventive Cardiology Academic Awards.

Furthermore, probably the single most important stimulus to encourage young scientists to embark on a research career is that of a perceived stability in grant support for meritorious research in the coming years. This is the intent of the stabilization of research project grants that we have discussed with the Committee previously.

Question: What funds have been set aside for the training of the next generation of research professionals in the field?

Answer: In 1982 we expect to provide $27.8 million for all forms of research training in support of some 1,550 full time equivalent trainees (about 50% of these are MDs). $25.3 million to support 1,374 full time equivalent trainees is estimated for 1983.

Question: How can more individuals be encouraged to pursue a career in heart, lung, and blood research?

Answer: We have already discussed the need for a reasonable expectation of a stable future as a primary requirement for a career in research. This means that not only must training programs be available and well-funded, but that investigator-initiated research grants should be stabilized at an appropriate level. It is also becoming apparent that the facilities and equipment necessary for modern training and research are becoming seriously delapidated, even at the Nation's leading academic institutions. The frustration experienced by an inability to perform increasingly complex investigations of high promise requiring increasingly sophisticated instrumentation, may well act as a serious deterrent to those thinking of a career in biomedical research. Improvements in research facilities are likely to have significant effects in increasing the pool of research manpower eventually available. Although the disincentives to a career in research are numerous and complex, the fundamental problem remains one of discouragement of the young doctoral graduate by a general concern about national goals in biomedical research support.

Question: What about non-Federal or non-Governmental sources of funding that could be tapped to expand the pool of researchers?

Answer: As discussed at last year's hearings, as NIH funds for training have been cut back, some increase in this activity has been undertaken by hospital administrators. Their emphasis, however, has been on patient care, and while this is entirely appropriate in the hospital setting, there remains concern about the relatively limited set of experiences afforded the trainee. New developments in recombinant DNA and hybridoma technologies are providing industry with possibilities for considerable expansion, and business investments in biomedical research are increasing accordingly. However, the extent to which these new ventures will provide opportunities for training is as yet unclear. Furthermore, industrial goals and priorities will not always coincide with academic objectives and the public interest. There are at least two reasons why support of training by the private sector--even to the extent it may be available--may be less desirable than that from the Federal government. First, business responds rather quickly to market pressures, leading to a possible lack of long-term stability, already emphasized as an important consideration for those contemplating a research career. Second, Federal support of training, particularly in the case of the institutional grant, allows a certain standard of quality and scope of research experience to be provided for the trainee, since specific and uniform approaches of this nature may be required of the recipient institutions. However, the commercial sector is prone to provide inducements to the promising trained investigator and direct him or her from the avenues of intellectual curiosity and areas of fundamental scientific breakthrough to areas of specific commercial need. The commercial sector is unlikely to provide support for research training unrelated to its immediate or foreseeable needs.

HYPERTENSION THERAPIES

Question: When the cause of hypertension cannot be determined, to what extent can a patient's blood pressure be controlled by known therapies?

Answer: The abnormally elevated blood pressure of essential hypertension can almost always be controlled if sufficient care is taken. Modern drugs operate through several different mechanisms, and either alone or in combination, they are effective in lowering the blood pressure to normal or to values close to normal even when hypertension is severe. Non-pharmacological therapies, particularly weight loss, salt restriction, and exercise, are also important contributors to the management of hypertension in many patients; they need considerable further explanation.

Question: Is such therapy successful in preventing the complications of hypertension?

Answer: The treatment of hypertension will significantly reduce the complications of hypertension such as stroke, heart attack, eye damage, and renal and heart failure. Several studies including the High Blood Pressure Detection and Follow Up Program have reported fewer fatal and non-fatal cerebrovascular events among the systematically treated patients, even those with mild hypertension. Nonfatal strokes were reduced by 31% for stepped care compared with referral care. There were also fewer stepped care participants developing the complication of left ventricular hypertrophy as noted on the fifth year electrocardiogram compared with the base line. Certain risk characteristics for premature death and related to ischemic heart disease--such as the history of severe chest pain as documented by the Rose Questionaire, reported heart attacks at annual interviews, and electrocardiographic changes at five years consistent with the Minnesota Code Category for Myocardial Infarction--all had similar trends for fewer events in stepped care compared with referred care participants.

Question: Has any progress been made in determining the cause of the disease for this group of patients?

Answer: No single cause has been identified as the cause of essential hypertension. However, it has become clear that hypertension can result from several different mechanisms and the interplay among them. Genetics is important and studies of families, of twins, and in animals indicate that perhaps half or more of the variability in blood pressure is heritable. Environmental factors such as excessive sodium in the diet and a low socioeconomic status are also correlated with hypertension. From the point of view of mechanisms several neural and humoral pathways that affect the heart, the blood vessels, and the blood volume and water balance of the body have been implicated as mechanisms that play a role in setting the level of both normal and abnormal blood pressure. Work is proceeding to relate more closely the role of the individual parts of this complex of mechanisms to particular examples of high blood pressure. Understanding the causation of the disease is of highest priority in developing strategies of prevention and has highest priority in the Institute's long term plans.

SERUM CHOLESTEROL LEVELS

Question: What attention have you given to the recent evidence suggesting that low serum cholesterol levels may contribute to an increased incidence of colonic cancer in men?

Answer: From the first appearance of such reports, the staff of the NHLBI have sought out information to determine the validity of the reported possible association of low serum cholesterol levels and increased incidence of cancer of the colon in men. Intensive analysis of data from all of the major population studies was carried out to look for any such relationship of low cholesterol to death from all forms of cancer, including cancer of the colon.

Preliminary data from eight epidemiological studies were reviewed with a panel of experts in February 1980. Three of the studies (Framingham Heart Study, the Puerto Rico Heart Study, and the Honolulu Heart Study) showed a statistically significant association of low cholesterol levels and cancer mortality; however, this was not found in the other five studies reviewed.

A further intensive search for other population data was carried out. More than 50 investigators in the United States and in other countries who had population studies were contacted and asked if they could provide data to investigate such findings. Seventeen studies were able to conduct such an analysis and the investigators were invited to present their findings at a Workshop on Cholesterol and Non-Cardiovascular Disease Mortality on May 11-12, 1981. More than 120 researchers attended this Workshop providing a much larger amount of information for review than was previously available. Eight of the seventeen major studies presented at the Workshop found an inverse association between serum cholesterol and malignant neoplasms in men. None of the studies found a significant association between cholesterol concentration and incidence or mortality from cancer in women.

Only four studies found a significant inverse association with colon cancer in men (Framingham, Honolulu Heart Study, Stockholm, and Hiroshima-Nagasaki Studies). Because of the inconsistencies of the findings among this major group of studies the Panel agreed that the correlations observed did not substantiate any direct cause and effect relationship between low plasma cholesterol levels and cancer.

Various speculations about possible mechanisms to explain an association between very low cholesterol concentrations and colon cancer were offered; however, no basic knowledge from other research could satisfactorily explain these findings.

There was agreement among the panel members that the findings do not present a public health challenge; however, they still present a scientific challenge. It was also the unanimous opinion of the panelists that the data did not preclude, countermand or contradict the current public health message which recommends that those with elevated cholesterol levels seek to lower them through diets lower in saturated fat and cholesterol. While there is inconsistent but confirming evidence of a possible increase in cancer risk at very low cholesterol levels (below 180 mg/dl) in men, the magnitude of this risk is generally modest when present. Physicians can feel confident in advising reduction of blood cholesterol levels for all persons with higher than average levels.

A summary of the Workshop's findings and recommendations was produced and has been distributed to a wide number of researchers who are known to have interest in this subject. A summary also was reported in the Journal of the American Medical Association in August, 1981. Wide publicity to these findings has also been sought and the Workshop findings have been reported in Science and in the public press.

A major presentation on Cholesterol and Non-Cardiovascular Mortality was given at the 55th Scientific Sessions of the American Heart Association on November 17, 1981, by Dr. Robert Levy, former Director of NHLBI.

The Workshop and the findings from this large group of studies are now known to a wide range of researchers in cardiovascular disease and in cancer research. It is anticipated that this will stimulate further research on this question. For the present we do not find the available evidence of a possible association of very low cholesterol levels below 180 mg/dl and increased incidence of colon cancer in men of special health concern. No changes of current advice are needed and we continue to encourage reduction of high cholesterol levels for persons who have high levels because of the established high risk of developing coronary heart disease.

Question: A recent report of a Japanese Study indicated that the drug "Compactin" lowered the serum level of cholesterol when administered to patients with very high blood cholesterol levels. Has the drug Compactin been studied in the United States and, if so, when might we expect to see results of these studies?

Answer: Compactin is a member of a new group of cholesterol-lowering drugs (HMG CoA Reductase Inhibitors). Compactin was developed by a Japanese pharmaceutical company and to our knowledge, no clinical studies have been initiated in the United States. Limited clinical studies elsewhere suggest that it is a powerful cholesterol-reducing agent, especially in combination with another class of cholesterol-lowering drugs, the biliary sequestrants. A report of serious animal toxicity (cancer) has inhibited assessment of Compactin and related compounds. Caution is also required since the drug's mode of action raises the possibility of other types of toxicity. A United States company has developed Mevinollin, a drug with similar properties. A very limited number of clinical studies have proceeded with a view to the toxicity question, but none have yet reported their findings.

It is likely that other members of this class of drug are under development, some of which may reach clinical assessment. Compactin has been reportedly synthesized, also making it likely that many derivatives will appear.

DISEASE PREVENTION AND HEALTH PROMOTION

Question: A number of large corporations have established early detection programs for their employees in cooperation with your Institute. The anticipated savings in terms of lost productivity and long-term health care costs could be significant. What type of impact are worksite-sponsored disease prevention and health promotion programs having?

Answer: The overall impact of these programs appears to be quite favorable. Many companies with worksite programs have reported less absenteeism, less use of sick leave, and less hospital and disability costs. NHLBI's involvement in this area has been to study, help develop and help implement worksite programs designed to reduce cardiovascular risks. Most of our experience has been with high blood pressure control programs and the indicators in this area are also quite favorable. At the same time, we still need more data to conclusively assess the cost-savings implications of these programs as well as the impact on cardiovascular morbidity and mortality. That is why we have supported three three-year studies--at Ford Motor Company, Westinghouse, and the University of Maryland. These studies have recently ended and the data are now being gathered and analyzed. We hope the final reports will give us additional insight into the value of the worksite in disease prevention.

Question: To what extent should this type of orientation be encouraged?

Answer: We feel it should be vigorously encouraged and have given it priority as a major disease prevention activity. During the past few years, we have helped many companies begin high blood pressure control or cardiovascular risk reduction programs. We have an ongoing working relationship with such companies as Campbell Soups, Johnson and Johnson, and Kimberly Clark. We have assisted companies such as General Motors, Boeing Aircraft and American Telegraph and Telephone in initiating or improving worksite programs. One gratifying aspect of growing private sector involvement in this area is that many companies are now promoting the concept of worksite programs among their peers in industry. We have also jointly developed seminars related to cardiovascular health at the worksite with both the American Occupational Medical Association and the American Association of Occupational Health Nurses. In the voluntary sector, we provided assistance to the American Heart Association in the design and implementation of that organization's promotion effort to establish high blood pressure control at the worksite.

Question: Is this the best mechanism for reaching the public?

Answer: It certainly represents an effective way of reaching a broad segment of the public. There are certain characteristics in the worksite environment which are hard to duplicate elsewhere. In a sense you have a captive audience. Generally, there is less difficulty in making sure individuals keep appointments with physicians or occupational nurses. It is also usually easier to follow-up with patients to make sure they are following their treatment programs. For example, in many worksite programs, as many as 80 percent of hypertensives are adhering to their treatment regimen. In community-based programs, the compliance rate is usually about 20 to 25 percent. Frequently, peer encouragement at the worksite is of value in obtaining patient cooperation.

Just how effective worksite programs will become as a major means of reducing disease risks and promoting healthy lifestyles is difficult to gauge. One determining factor will be the number of companies which will adopt such programs in the future. To a large degree, that number will depend on the evidence which is gathered regarding the value of such programs. If the current trend continues and more companies get involved in disease prevention and health promotion, the worksite will likely become an exceptionally important place where we can help reduce disease and premature death.

Question: Can these programs be promoted through insurance companies?

Answer: Yes they can and they are. Insurance companies are getting involved in a number of ways. More insurance companies are now offering or considering reduced premiums for nonsmokers and controlled hypertensives. In fact, we jointly developed with the Association of Life Insurance Medical Directors the report, "The Underwriting Significance of High Blood Pressure," which insurers have used as a source for reducing premiums for controlled hypertensives. This association of medical directors very recently became a member of the Coordinating Committee of the National High Blood Pressure Education Program, which we administer. We contracted with Blue Cross/Blue Shield for a pilot study in which they used their representatives to market high blood pressure control programs among their group subscribers in two states, Connecticut and Michigan. The results were impressive. On the basis of this demonstration study, Blue Cross/Blue Shield is now promoting worksite programs to their group subscribers throughout the nation. Upon request, we provided technical assistance to Travellers Insurance Company to help develop model high blood pressure control programs at the worksite among group subscribers in Florida and New Jersey. After their programs are tested, Travellers intends to also go nationwide with the program. We have also assisted Metropolitan

Life in developing its Center for Health Help, a model disease prevention/health promotion program.

On the basis of ongoing conversation and consultation with a number of insurance companies, we are optimistic that their role in stimulating worksite programs is an expanding one.

Question: How are the unemployed reached?

Answer: While the worksite represents an effective avenue to reach a great many Americans, it certainly is not the only avenue, and it obviously is not the route to take to reach the unemployed. We carry out a national education program for both the lay public and the health professions. We provide technical assistance and/or information to every State and to more than 2,000 community based high blood pressure programs. Many of these programs are directed towards minority or disadvantaged populations where unemployment is most serious. An advisory group with representatives from minority populations and organizations provides counsel to our overall national high blood pressure control program. We have several demonstration programs in both rural and urban areas to test and develop improved methods of carrying out high blood pressure control programs for those segments of the public where unemployment is especially high.

OVERVIEW MATTERS

Question: We've seen a table indicating that the Heart, Lung and Blood Institute appears to be the third slowest growing Institute on the NIH campus in budgetary terms. The table shows that since 1977 your budget has increased by 45.5 percent while others have gone up far more. Are you satisfied with this record, or do you believe the increase in funding should be greater so that you are in a better position to address priority and break-through areas?

Answer: Naturally we are disappointed that each year since 1976, NHLBI has been at or near the bottom in annual percent growth among our sister Institutes. (In constant dollars the 45.5% increase of FY 83 over FY 77 is actually a decrease in excess of 18%).

Priority in break-through areas are typically exploited most rapidly and advantageously through Institute initiatives, particularly in the form of research and development contracts. Looking back over recent years, between FY 75 and FY 82 the dollars spent on Institute-initiated awards fell from 47% to 28% of our extramural program. Most of this decline took place in R & D contracts (especially in clinical trials) which decrease almost along a straight line from 29% to 12% of our extramural program. The other component of Institute initiated activities, centers and other grants in response to Requests for Grant Applications, has remained relatively constant throughout this period at about 16% of extramural funds. During this same FY 75 to FY 82 period, the fraction of extramural funds going to investigatorinitiated grants has increased almost linearly from 44% to 63%; this has been necessary to fund as large a fraction as possible of our priority programs in the regular grant area. Nevertheless, we have had a progressive decline in award rates from 56% of approved grants in FY 75 to 35% projected for FY 82.

If additional resources had been available we could have allocated more to priority areas, and we would have been more supportive of topics offering promise of break-through.

Question: To what extent will your budget permit you to continue to support timely and important scientific initiatives through Institute-solicited programs?

Answer: Looking to FY 83 we see an award rate of 25% of our favorably recommended investigator-initiated grants and no opportunity for institute-solicited programs.

CLINICAL TRIALS

Question: What clinical trials did you initiate--or terminate--in the last year? What clinical trials would you like to do in the year ahead?

Answer: The Institute has not initiated a full scale clinical trial since FY 78.

In FY 81 we initiated the pilot phase of the clinical trial on Systolic Hypertension in the Elderly to determine whether and how we can achieve blood pressure control without serious side effects. Depending on the outcome of the pilot study, the definitive trial to determine whether this is of therapeutic benefit in terms of improved life expectancy will be ready for implementation in 1984. It will require substantially larger numbers of patients and greater costs. In FY 82 we are planning to start a pilot study on antiarrhythmic agents in the prevention of sudden cardiac death. Definitive scale studies to truly test the effectiveness of these drug regimens upon mortality would not begin for several years.

In the past year we terminated one of our most successful studies, the Beta-blocker Heart Attack Trial (BHAT). This study, involving over 3,800 patients, showed that the beta-blocker, propranolol, when taken on a regular basis by survivors of a heart attack, resulted in a significant decrease in mortality compared to patients taking a placebo. When followed for periods of twelve to thirty-nine months, mortality was 9.5% in the control group and 7.0% in the treated group--a 26% decrease in mortality. These definitive results became available 9 months before scheduled completion of the trial; they were promptly announced and the trial stopped. Beta-blockers such as propranolol are suitable for probably three quarters or more of patients who survive a heart attack and a significant impact on the saving of life can be expected.

In FY 81 we also completed an investigator-initiated collaborative clinical trial on the management of a common congenital heart disease, patent ductus arteriosus. In infants born with this lesion in whom the lesion did not close spontaneously, the use of the drug, indomethacin, cut the need for surgery from 70% to 30%. This is one of the most common needs for surgery in the neo-natal period.

In FY 81, the first major clinical trial of a new vaccine to prevent type-B hepatitis is now completed. The vaccine, which provides virtually full protection against this severely debilitating disease, consists of highly purified, formalin-inactivated virus subunits, derived from the blood plasma of chronic carriers of hepatitis-B. For this study, a population of more than 1,000 healthy young male volunteers at high risk of contracting the disease were randomized into two groups, one to receive the vaccine, the other a placebo. In those given the vaccine, 90 percent developed antibodies against hepatitis-B virus after two injections; this rose to 96% developed antibodies against hepatitis-B virus after two injections; this rose to 96% after a third injection. Of those given the placebo, less than 6% developed antibodies spontaneously.

In FY 80 several major clinical trials were completed, including the Hypertension Detection and Follow-up Program (HDFP), the Nocturnal Oxygen therapy trial and the prevention of neo-natal respiratory distress. (For this latter trial, follow-up is continuing to make sure that the prevention of the respiratory distress syndrome, which is successfully achieved by the use of sterioids near the termination of high risk pregnancies, is not accompanied by long term adverse side effects. For HDFP we have a 3 year late follow-up to see how these patients fare after the detailed trial.)

Clinical trials of particular importance at this time include a definitive study to assess the possible effectiveness of intracoronary and intravenous thrombolytic therapy in the treatment of acute myocardial infarction. Over the last eighteen months or so there has been great interest in the use and efficacy of emergency cardiac catherization in patients with symptoms of acute myocardial infarction and, in those found to have occlusion of the coronary artery, the immediate infusion of an enzyme which often leads to the break up of much of the coronary thrombus. The coronary angiographic changes with this infusion are dramatic and there is a plausible rationale why there may be net clinical benefit. However, there has been no study which establishes true clinical benefit in terms of lives saved or significant preservation of heart muscle being kept from irreversible damage. The procedure is going into widespread use without validation. It is one of significant expense and requires considerable resources both in terms of apparatus and availability of personnel. An objective assessment of the value of the therapy is critically important.

The results of the beta-blocker heart attack trial have demonstrated the effectiveness of beta-blocker in the prevention of recurrent heart attack and death following myocardial infarction. It is now plausible to ask and important to test whether such therapy might not also be effective in preventing first heart attack and preventing sudden cardiac death in persons at high risk of sustaining heart attack. This can only be answered by a collaborating clinical trial.

The registry on percutaneous transluminal coronary angioplasty (PTCA) discussed earlier has provided data on the degree of effectiveness and safety of the procedure acutely. However, there are no significant data of long term effects; nor are there objective comparative studies against alternate forms of therapy in comparable clinical circumstances. A multi-center collaborative prospective trial of PTCA is of significant importance.

A clinical trial on ventilation perfusion scans and pulmonary angiography for diagnosis of pulmonary embolism is important in developing much more widely and easily applicable, reliable techniques for the diagnosis and assessment of pulmonary embolism, a condition which is thought to be associated with at least 50,000 and possibly a substantially larger number of deaths annually.

As indicated above, the pilot stages of clinical trials on isolated systolic hypertension in the elderly and on antiarrhymthic agents in the prevention of sudden cardiac death have been or are being initiated; when these are complete (after FY83) full scale studies will have to be undertaken to answer the definitive questions of efficacy.

Question: Could you please compare the award rate and number of awards for investigator-initiated grants currently and over the past few years? In your opinion, what implications do you believe this policy or trend, if it is a trend, has for NHLBI research?

Answer: There has been a progressive downhill trend in the award rate for favorably recommended investigator-initiated grants. For example, in 1970 73% of the favorably recommended grant applications received awards. Referring to the period since 1975 discussed above, the award rate has fallen in a bumpy but progressive downhill fashion from 55% in FY 75 to an expected 35% in FY 82 and a projected 25% in FY 83. As noted above, between FY 75 and FY 82 funds for investigator-initiated grants have increased from 44% to 63% of our extramural program portfolio. The decreasing fraction of awards has taken place despite this realignment of resources.

With respect to the number of awards, in the three years FY 77 through FY 79 we were able to award an average of 810 competitive renewal and new awards annually. In FY 83 we foresee the award of 545 such grants.

NATIONAL INSTITUTE OF DENTAL RESEARCH

STATEMENT OF DR. JOHN F. GOGGINS, ACTING DIRECTOR

ACCOMPANIED BY:

- **DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH**
- **DR. RICHARD L. CHRISTIANSEN, ASSOCIATE DIRECTOR, EXTRAMURAL PROGRAMS**
- **DR. MARIE U. NYLEN, DIRECTOR, INTRAMURAL RESEARCH**
- **DR. JAMES P. CARLOS, ASSOCIATE DIRECTOR, NATIONAL CARIES PROGRAM**
- **GILBERT D. PRESS, BUDGET OFFICER**
- **NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH**
- **JOHN PATTERSON, EXECUTIVE OFFICER**
- **ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. Our next witness is Dr. John Goggins, the Acting Director of the National Institute of Dental Research.

Dr. Goggins, it is a pleasure to have you with us. Introduce your colleagues and summarize your statement, and we will proceed with questions.

INTRODUCTION OF ASSOCIATES

Dr. GOGGINS. Thank you, Mr. Chairman.

To my immediate left is Mr. Gilbert Press, our Budget Officer. Sitting behind me is Dr. Marie Nylen, our Scientific Director. To her left is Dr. James Carlos, Associate Director for the National Caries Program. To his left, Dr. Richard Christiansen, Associate Director for the Extramural Programs. And sitting on the end is Mr. John Patterson, our Executive Officer.

Again, I want to thank you for the opportunity to come before you today on behalf of the National Institute of Dental Research. Oral disease represents a major burden on this Nation in terms of suffering and decreased quality of life, as well as in terms of fiscal burden placed upon the American people. This amounts to approximately $16 billion a year.

Since most oral disease is irreversible, prevention is the most important approach to maintenance of oral health. Therefore, NIDR's primary goal is the development of preventive methods through biomedical research.

All of us in this room appreciate the fact that biomedical research is a long-term investment. Senator Andrews made some comments on that this morning. Congress recognized this fact back in the days when they established the National Institutes of Health, and those investments today are paying rich dividends.

The National Institute of Dental Research is the third oldest of the Institutes at NIH, being established after the Cancer and Heart Institutes. They have already testified about the dividends that are being paid by research conducted in those areas.

DENTAL CARIES PREVALENCE SURVEY

Last year Dr. Scott reported to this committee that preliminary analysis of the national dental caries prevalence survey indicated that dividends were now being received from the investments in dental research over the years. Today I am pleased to report that a thorough analysis of these data has confirmed the preliminary indications. The prevalence of dental caries among school-aged children has decreased by approximately 30 percent between the early 1970's and early 1980's. This represents a huge savings to the Nation, both in terms of suffering prevented and in dollars saved.

PERIODONTAL DISEASES

While considering this advance in our work, for which we feel justly proud, we also recognize the need for continued research. Progress continues to be made in developing new and improved means to further reduce the prevalence of dental caries. Studies of periodontal diseases are yielding important information about the bacterial agents that cause these diseases and on the mechanisms by which the supporting structures of the teeth are destroyed.

CLEFT LIP AND CLEFT PALATE

Basic studies of the development of the head and face are providing us with knowledge that hopefully will lead to the identification of factors contributing to the cause of cleft lip and palate. This information should ultimately open paths leading to prevention.

Senator SCHMITT. Does the cleft lip and cleft palate seem to have a potential cure?

Dr. GOGGINS. No, prevention.

Senator SCHMITT. I should have said prevention. It would have to be during pregnancy, right?

Dr. GOGGINS. Yes; the palate closes sometime before the 9th or 10th week of pregnancy.

Senator SCHMITT. Is that thought to be a genetic thing?

Dr. GOGGINS. They're finding a combination of factors. The general theory is that there may be a minor genetic predisposition and this, in combination with environmental factors, may result in a cleft lip or palate.

Senator SCHMITT. So environmental attack such as——

Dr. GOGGINS. Such as a teratogen or certain drugs, such as Dilantin, which is used for treatment of epilepsy. There has been an indication that there is an increased incidence of cleft lip and palate in children born of these mothers.

Senator SCHMITT. Anything more common such as cigarette smoking or using alcohol?

Dr. GOGGINS. I really don't know if there are firm data on cigarettes. I think there is a clear indication of alcohol's relationship with developmental anomalies. Perhaps Dr. Christiansen can provide us with more details.

Dr. CHRISTIANSEN. Alcohol can cause deformity quite early in embryonic development, much earlier than when clefting may occur. The incidence of clefts increases slightly with alcohol use by the mother. This is a recognized problem. That may be what Dr. Goggins was alluding to.

Senator SCHMITT. Is this new data, the correlation between deformity in general and alcohol consumption?

Dr. CHRISTIANSEN. The fetal alcohol syndrome, which may include multiple craniofacial defects, was described approximately 10 years ago. More and more evidence is coming in on this issue.

The one significant factor related to prevention, though, was one of the applications in animal studies where an increase in oxygen was instituted in the embryonic environment. The rodents which normally had a clefting rate of approximately 20 percent actually developed fewer clefts. So this is leading toward a preventive measure in an animal model system. Whether or not there is human application remains to be seen.

Senator SCHMITT. Which suggests if a particular drug which enhances a predisposition toward clefting, essentially you might have a preventing mechanism.

Dr. GOGGINS. That's right. Hopefully, through fundamental studies we will be able to identify those individuals who have a genetic predisposition to clefting, and we will also develop further knowledge of those agents that could make the difference between cleft and no cleft. With this kind of knowledge we would hope to be able to prevent clefting.

Senator SCHMITT. Please proceed.

ORAL HEALTH RESEARCH

Dr. GOGGINS. We also are making advances in the area of soft tissue diseases. For example, we are learning more on how the herpes virus, which infects millions of individuals and causes recurrent painful ulcers of the lip, wreaks its havoc. We are progressing steadily in developing therapeutic and preventive methods to attack this disease.

In summary, we see oral health research progressing on all fronts. We are learning more about the causes of the diseases and the biological mechanisms involved. With the passage of time, we are gaining the necessary knowledge so that our research today is becoming more and more clinically applicable, leading ultimately to the prevention of the major oral diseases.

We are confident that these efforts will continue to pay the rich dividends that the efforts we have made in the past are already paying.

Mr. Chairman, the NIDR budget request for 1983 is $74,462,000, and I will be pleased to answer any questions.

PREPARED STATEMENT

Senator SCHMITT. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. JOHN F. GOGGINS

I appreciate the opportunity to appear before this subcommittee to review the programs of the National Institute of Dental Research.

The National Institute of Dental Research, through studies conducted in its Bethesda laboratories and through grants and contracts, supports the major portion of dental research within the United States.

The magnitude of the Nation's burden arising from oral diseases is a matter of record. Experience has shown that the problems of oral diseases cannot be met by improvements in treatment alone. The untreated decayed teeth, the high levels of periodontal disease, the large number of children born each year with facial deformities, the high incidence of painful recurrent oral ulcerations, all attest to the critical need for research that will contribute new knowledge of the diseases of the mouth and face and of their control. Prevention is, therefore, of the utmost importance in oral health because, unlike those diseases successfully cured by medical treatment, oral health problems are largely irreversible.

Dental Caries

Dental caries has been accurately described as the most universal, chronic and costly of all non-fatal human diseases. While advances in caries research are heartening and a substantial reduction in the prevalence of caries has been achieved, the public cost of this disease still is estimated to be more than $8 billion per year. Since its inception in 1971, the National Caries Program of the NIDR has worked to expedite community and individual use of preventive techniques that are already available while developing others that, when used coordinately, will lead to the control of this major public health problem.

The National Caries Program recently completed a nationwide survey to assess the prevalence of dental caries in school-aged children. Examinations of approximately 40,000 children served as a sample to represent the 48 million U.S. children in kindergarten through grade twelve. The results of the survey indicate that dental caries in the school population has decreased by an estimated 25-30% in the past decade. It is likely that a number of factors have contributed to this improvement in the dental health of children. Among these factors are the use of community water fluoridation, fluoride toothpastes and the dramatic growth in school-based programs of weekly mouthrinsing with fluoride solutions or the daily use of fluoride tablets.

A prototype device that releases controlled levels of fluoride inside the mouth for extended periods of time has passed animal trials and limited human trials and is now ready for longer term clinical trials. When available, such a device should provide protection against tooth decay in especially vulnerable individuals; e.g., children who, because of handicap or disability, cannot effectively clean their teeth.

Studies are underway to define the characteristics of foods and the eating patterns that lead most strongly to caries in school children. In addition, animal studies have been undertaken to identify factors in foods that can modify their decay-causing potential. Meanwhile, the search continues for a safe, non-cariogenic alternative to sucrose for use in snacks and other foods.

Steady progress continues in efforts to develop alternative approaches to caries prevention. Research continues toward the development of a safe vaccine to provide long-lasting protection against tooth decay and to find an acceptable route of administration. Bacterial antigens able to stimulate the body's defense mechanism have now been characterized; tests to measure immune responses have been developed; and brief clinical trials have shown that immunization through oral administration of the antigens is feasible.

Periodontal Diseases

Periodontal diseases continue to be a problem of increasing concern in our society. These diseases become more evident and more severe with age, but, contrary to common belief, periodontal diseases are not confined to the adult population. NIDR studies, which are contributing greatly to the understanding of the causes and the progression of this ubiquitous disease, hold promise of leading to significant improvements in control of the disease and to its eventual prevention.

Studies have continued to make progress in the identification of bacteria implicated in periodontal disease and are now beginning to reveal some of the mechanisms by which these bacteria may cause the disease. Certain strains of bacteria recovered from patients with localized juvenile periodontitis produce a substance that directly destroys the white blood cells which defend the body against bacterial infection. Expanded studies to determine how these bacteria can overthrow the body's defense mechanisms may lead to interceptive techniques to prevent the tissue-damaging effects of bacterial toxins.

Researchers have noted that patients with juvenile-onset, insulin-dependent diabetes mellitus have a higher prevalence of periodontitis than non-diabetic children. They have also found that periodontal disease tends to be more severe in patients with a longer duration of diabetes. Bacteriological investigations of periodontal lesions in diabetic patients have identified a group of characteristic organisms associated with the lesions. Preliminary studies have revealed that, when the periodontal health of the diabetic patient is improved by treatment, there is a reduction in acute diabetic complications with concomitant reduction in insulin requirement. If these studies are confirmed, the prevention and treatment of periodontal disease may contribute greatly to the improved medical and dental management of diabetic patients.

Hormone-like factors involved in chronic inflammation such as periodontitis have been isolated and purified. These molecular mediators serve as signals that lead to increased inflammatory response and eventually to tissue destruction. The eventual goal of these activities is to understand the role of these factors sufficiently to enable the manipulation of the inflammatory process using antibodies, drugs and/or the factors themselves. Through such studies we would hope eventually to be able to prevent the damage of the inflammatory process while enhancing the protective processes.

Soft Tissue Disease and Nutrition

The herpesviruses infect 50-70% of the population and have the unusual capacity to persist in a latent form in many individuals. Their subsequent reactivation often results in debilitating recurrences of painful ulcerations.

Researchers are providing tools to improve diagnosis and therapy in herpes infections although, to date, no antiviral drug has been effective in treating herpesvirus-caused lip infections (fever blisters or cold sores) mainly because existing agents seem unable to penetrate the human skin. To overcome this problem, investigators are pursuing new methods for delivering antiviral preparations directly to the infection site. While successful therapeutic measures should aid individuals during recurrences of the disease, prevention of initial herpesvirus infections by the use of a vaccine remains the most promising approach for ultimate control. Efforts are underway using molecular and biochemical techniques to isolate and purify highly specific antigens from the virus that will induce immunity without risk.

Degenerative changes occur in oral tissues as a result of irradiation, cancer chemotherapy and treatment with immunosuppressive drugs. Studies are being conducted to develop the means for predicting and preventing pathological tissue changes. Salivary flow characteristics appear to be useful for identifying early changes.

Craniofacial Anomalies

Neural crest cells are the most important contributors to the developing craniofacial region. The cells first develop along the back of the early embryo and then migrate long distances to eventually give rise to many of the oral facial structures. Basic studies now suggest that extracellular macromolecules guide the migrations of these and other embryonic cells and determine their localization in tissues and their patterns of differentiation.

Similarly studies on the healing of wounds have shown that extracellular factors attract cells to the traumatized region and then stimulate the cells to proliferate. When the role of such factors is fully understood, the potential for influencing the speed of the healing process and the preventing of untoward complications, such as excessive scar formation and wound contraction, will be enhanced.

Past theories have proposed that human malformations occur from an accumulation of minor genetic errors and damage from environmental toxins. Studies have shown that exposing mice to a reduced level of oxygen increased the incidence of cleft lip in the offspring. New studies reveal that increasing the oxygen supply to such mice reduces the incidence of the deformities. These studies show that a change in a single maternal environmental factor could influence malformation. Continued research on the factors that contribute to the cause of craniofacial malformations should lead to the eventual development of preventive procedures.

Relapse and alteration of growth are unfavorable sequelae that frequently follow surgical correction of dentofacial deformities. Both are related to a failure in the ability of the craniofacial musculoskeletal system to adapt to changes in form and function.

Primate studies promise to provide information which will have direct application to the stable correction of deformities in man.

Restorative Materials

Studies continue toward the development and testing of new biomaterials and devices so that function and appearance of the oral and facial tissues damaged by dental disease, congenital anomalies, and accidents can be more satisfactorily restored.

Following preliminary animal experiments to test a cylindrical titanium implant, investigators have conducted a 4-year clinical evaluation of such implants in extraction sites in primates. Free-standing implants and implants used for support of bridges performed equally well with relatively few complications. Similar studies in a limited number of human patients will now be initiated. Also, clinical trials in humans of a titanium blade-implant to serve as an abutment for a fixed partial denture will soon be underway.

Because of the increased substitution of base-metal, nickel-chromium alloys for gold in crown and bridge prosthetics, researchers have launched a study to determine if these alloys may induce sensitivity reactions in certain patients.

Pain Control and Behavioral Studies

Promising studies of the way that chemical agents affect psychological states of dental patients involve endorphins--the analgesic, morphine-like compounds produced by the brain--which reduce pain experience. Previous studies have shown that clinical pain itself stimulates the release of pain-relieving endorphins within the brain. Evidence now indicates that the placebo effect, by which a patient taking an inactive substance experiences relief from pain, may also work through the endorphin system. Narcotic analgesics also exert their effects through this same neural system. Continued studies of the body's own intrinsic pain-modulating system and its interaction with specific analgesics could lead to the development of non-pharmacological approaches or to better drug combinations to relieve pain.

Further studies are planned to develop and maintain better oral health attitudes and behaviors needed to prevent oral diseases. Currently, the American public does not apply known preventive measures such as use of fluorides and diet modifications to full advantage. Investigators have shown that commonly used measures of health attitudes do not predict which children will follow a specific regimen of home oral health care. Some behavioral interventions, such as tangible rewards, did substantially increase compliance with the home oral hygiene procedure.

An estimated 10% of our population avoids needed dental treatment because of excessive fear. Ongoing research into dental fear and anxiety is expected to result in simplified and improved procedures that will allow dentists to treat these patients on a new level of behavioral expertise.

This concludes my prepared statement. The budget request for fiscal year 1983 is $74,462,000. I will be pleased to answer any questions you may have.

Biographical Sketch

NAME:	John F. Goggins
MOST RECENT POSITION:	Acting, Director, National Institute of Dental Research
BIRTHPLACE AND DATE:	Flint, Michigan; October 26, 1933
EDUCATION:	Predental, University of Notre Dame, 1954 D.D.S., Marquette University, School of Dentistry, 1958 M.S., Marquette University, 1965
EXPERIENCE:	Acting Director, National Institute of Dental Research, NIH, 1982- Deputy Director, National Institute of Dental Research, NIH 1981- Associate Director for Collaborative Research, National Institute of Dental Research, NIH, 1974-1981 Chief, Periodontal and Soft Tissue Diseases Program, National Institute of Dental Research, NIH, 1973-1974 Staff Scientist, National Institute of Dental Research, NIH, 1966-1973 Postdoctoral Fellow, National Institute of Dental Research, NIH, 1965-1966 Instructor, Department of Pathology, Marquette University, School of Dentistry, 1964-1965 Graduate Student, Marquette University, School of Medicine, 1963-1965 Private Practice, Flint, Michigan, 1960-1963 General Dental Officer, USAF, 1958-1960
ASSOCIATION MEMBERSHIPS:	American Association for the Advancement of Science American Dental Association American Association for Dental Research (Councilor) International Association for Dental Research Histochemical Society
SPECIAL AWARDS CITATIONS, OR PUBLICATIONS:	Alpha Sigma Nu U.S. Public Health Service Commendation Medal Author of some 20 publications

NUTRITION

Senator SCHMITT. Thank you.

Would you discuss briefly a little bit more of your work in nutrition as it relates to the dental problem?

Dr. GOGGINS. We have several grants in nutrition. There are a limited number of directly identifiable connections between oral diseases and nutrition as far as nutrition being the causative factor is concerned.

Diet, of course, represents a major area in caries prevention with the association between sugars and the production of acid as a cause of dental caries. This is in the area of diet.

In the area of nutrition, we are doing some fundamental studies that indicate that there could be a relationship to disease and disease resistance levels, but not necessarily as the primary etiology. For example, some studies conducted in primates have shown that a subclinical deficiency of vitamin C resulted in an increased susceptibility to periodontal disease, and also decreased ability of the white blood cells of the animals to fight infection. So here we are looking at a situation where a subclinical vitamin deficiency could indeed be related to increasing susceptibility to a disease—not necessarily the cause. Also, folic acid deficiencies have shown increased permeability of mucous membranes which could again decrease one's resistance to infection.

These are the general areas of current research. We are looking for nutritional contributions to disease. We don't have any data to date that would indicate that these diseases are nutritional in their etiology.

Senator SCHMITT. Do you think there's any possibility that the enhancement of the school lunch programs and other child nutrition programs during the same period of time that you have seen your increase in fluoridation could be responsible for the decrease in caries?

Dr. GOGGINS. I really don't know how to answer that. The school lunch programs may be preventing the children from eating a lot of sweet snacks at lunch time—eating more nutritious foods rather than snacking at lunch time. I don't think that nutrition, that is, the fuel for the body, is directly related to dental caries after the teeth have developed and erupted. But as I said before, diet can be related to caries.

Senator SCHMITT. If you have ever visited a school lunchroom, you know it's going to be awfully hard to run that test.

Dr. GOGGINS. I know. My son has told me about the school lunchroom.

Senator SCHMITT. I still think my lunch pail was better.

INDIRECT COST OF RESEARCH GRANTS

Do you have any unique aspects in the Dental Research Institute relative to the cap on indirect cost of research grants other than what has been mentioned before?

Dr. GOGGINS. No; all the other Institutes have pretty much covered the impact issue. Our situation is quite similar. We have had to take a hard look at everything, and I would say we all seem to be in about the same boat.

RESEARCH CENTERS

Senator SCHMITT. How many research centers do you have?

Dr. GOGGINS. We have five broad research centers, multidisciplinary centers, and we also have three periodontal clinical research centers. The five centers are the programs that have been in existence now for 10 or 15 years. The clinical periodontal research centers were started about 5 years ago.

Senator SCHMITT. And will the level of effort there stay about the same this year, in fiscal 1983?

Dr. GOGGINS. In 1983? They will be staying level. They are currently taking a bit of a dip in funding due to the budget constraints under the continuing resolution. We plan to continue funding them. They will go up a bit on our 1983 budget to about $7.3 million for the multidisciplinary centers. Their budgets have remained at this funding level since about 1975 or 1976, so they will have to continue to tighten their belts to conduct the work they are doing.

CARIES VACCINE

Senator SCHMITT. What is the status of the caries prevention vaccine?

Dr. GOGGINS. We are still working on an anticaries vaccine, and we are making progress. Major efforts are being conducted right now to test different antigens. We have recently started some tests in primates, utilizing glucosyltransferase, which is an enzyme associated with the cariogenic organism, Streptococcus mutans, which contributes to the virulence of this organism. We have started tests in primates using this enzyme as an antigen. Other tests are being conducted to try to optimize routes and schedules for immunization.

We reported last year of preliminary tests in humans taking oral preparations of killed Streptococcus mutans, and the fact that these elicited positive salivary antibody responses. But before we can get to the point of having a major caries prevention clinical trial, we will have to develop the ultimate purified antigens to be used, the optimum schedule to administer it, and so forth. I expect that will be some years to come, but we are still making significant progress in this direction.

SUBMITTED QUESTIONS

Senator SCHMITT. Thank you, Doctor. I appreciate the testimony. We will have some more questions for the record.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

CONSTANT DOLLARS

Question: In terms of constant dollars, how does your 1983 budget compare with the purchasing power you had in fiscal 1973?

Answer: In 1973, the NIDR budget was $46,991,000. By contrast, its 1983 budget in terms of constant dollars is $33,829,000, a decrease of 28% in real purchasing power over the last 10 years.

DECREASE IN DENTAL CARIES

Question: How much more of a decrease in dental caries can we expect over the next five years? What needs to be done to speed up the progress?

Answer: Our recent nationwide survey of caries prevalence among school children demonstrated a decrease in caries of approximately 30 percent during the period 1972-80. There is strong presumptive evidence that this is due to preventive programs, particularly those involving fluoride administration in various forms. For example, the number of children involved in school-based, self-applied fluoride programs increased by over 10 million during the 1970's and is continuing to grow. Therefore, further decreases in caries prevalence can be expected during the next 5 years. The amount of this decrease, and the rate at which it will occur, depend upon several factors:

- Expanded and successful efforts to educate the public about the cost-benefit of fluoride programs -- both community water fluoridation and school-based topical fluorides.
- More widespread use of adhesive sealants to prevent caries on occlusal surfaces of teeth. A reduction in the cost of delivery of this regimen will be necessary.
- Success in presuading the public, especially children, to sharply reduce the frequency of intake of sugar-containing foods.

These factors, together with the availability of improved preventive methods still under research (including slow-release delivery system, sugar substitutes and vaccines) have the potential to rapidly reduce caries as a public health problem in the U.S. The immediate need is to convince the public to use the preventive methods already available.

PERIODONTAL DISEASES

Question: Now that we are having some success in reducing dental caries, what can we expect with regard to periodontal disease?

Answer: The possibilities for periodontal diseases control do not at this time parallel the recent successful results of caries research in reducing and/or controlling tooth decay. To date, the primary thrust of periodontal disease research has focused on elucidating the cause and basic tissue destructive processes involved. To that end, a major portion of the grant funds available in recent years have been awarded for studies to expand our understanding of the complex bacterial cause of periodontal diseases and the host's response to these diseases. As a result of knowledge gained in these two areas, preliminary studies are currently underway to develop suitable measures to control periodontal diseases and to ultimately prevent the diseases. These studies seek to develop antimicrobial agents to neutralize the disease-causing agents. Until effective antimicrobial techniques can be developed, continuing studies of traditional mechanical oral hygiene measures are being conducted to define the most effective combination of patients' home care procedures and professional office maintenance treatments.

Studies of host response mechanisms have shown that white blood cell deficiencies are associated with cases of specific types of periodontal breakdown. Continued research may lead to methods of curing such defects and thereby improving the protective functions of these cells.

COST OF PERIODONTAL DISEASE TREATMENT

Question: How much is spent annually to treat periodontal disease?

Answer: We have no accurate figures on the total amount spent to treat periodontal diseases, but data published in 1979 estimated that Americans spent over $800 million in 1977 (on prophylaxes $723 million and periodontal services $78 million by general practitioners). If specialists (periodontists) had been included in that study, the amount would have been even greater. The figure would be significantly higher today considering inflation and the increased number of older Americans.

DENTAL RESEARCH INSTITUTES AND CENTERS

Question: Please give us some examples of major accomplishments of your research centers over the last seven years.

Answer: The five Dental Research Institutes and Centers (DRICs) at the University of Alabama, Michigan, North Carolina, Pennsylvania and Washington have developed comprehensive basic and applied research programs of high quality that serve to underpin dental research throughout this country. These programs contribute on the order of 300 publications to the scientific literature each year.

The DRICs have attracted excellent scientists from disciplines not traditionally associated with dental research; their programs have now evolved to the point that these scientists are making significant contributions to the solution of oral health problems. A microbiologist at the Alabama center who is a pioneer in the development of recombinant DNA technology serves as an excellent example of this approach. He has applied recombinant technology to identify the genetic factors that enable oral microorganisms to produce carious lesions in teeth. The research is now focused on the manipulation of these factors to develop microorganisms, which may be used to produce a caries vaccine.

A virologist at the Pennsylvania center serves as another example. This scientist's basic research program on viruses is evolving toward the development of a safe and effective vaccine for herpes simplex virus infections, the extremely painful and debilitating condition which affects the lips and oral cavity. In a major step toward the goal, this scientist has isolated a molecular component of the virus, which, when injected into mice, made them immune to lethal doses of the virus.

A major aim of the DRICs is to enlist collaboration of all appropriate elements of the university in solving oral health problems. The Washington center presents a good example of how this aim is achieved. Center scientists and clinicians outside the center are collaborating to assess the degenerative changes that occur in oral and other tissues as a result of irradiation, cancer chemotherapy and immunosuppressive drug treatment in patients being given bone-marrow transplants. This research has resulted in better patient management by reducing some of the serious treatment side effects in cancer patients.

Another of the original aims of the DRICs was that they develop into centers of excellence. That this aim is being achieved is evident from the fact that each of the five centers has scientists regarded among the foremost in the world in such areas as connective tissue biochemistry, secretory immunology, oral microbiology and the molecular biology of plasmids.

AVERAGE COST OF GRANTS

Question: The average cost of a new competing grant for your Institute is less than the overall NIH average cost for competing grants. Why is this the case?

Answer: The NIDR grants program includes a larger percentage of young investigator awards, which have a ceiling of approximately $35,000 per year. The large number of these grants tends to reduce the average grant cost. Additionally, the NIDR provides a smaller percentage of its funds for the larger program project grants. Finally, the NIDR has made few awards that require funds for alterations or renovations which typically are very expensive cost items within the grant budget.

BUDGET CUTS

Question: Last year, you reported that if faced with a major budget cutback, there would have to be decreased funding in research training; applied research through the contract program; decreased intramural research; and decreased information-dissemination activities. If faced with a major budget cutback, what major program elements would you target for reduction in effort and which elements would you try to maintain or increase?

Answer: The Budget request for 1983 maintains a viable basic and applied research program and strikes a balance among its six categorical program areas. To accommodate a major cutback, the Institute would reduce its support for research in nutrition and acquired defects.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982 - and how much will you spend in fiscal 1983?

Answer: The NIDR supports five multidisciplinary Dental Research Centers and three Periodontal Research Centers. The amount of support was $9,178,000 in 1981, and is estimated at $8,699,000 in 1982 and $9,063,000 in 1983.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: Phase-out of several scientifically meritorious projects has already occurred within the Dental Research Institutes and Centers (DRICs) program as a result of recent fiscal contraints. The DRICs have been funded considerably below Council approved levels in recent years.

CLINICAL RESEARCH

Question: Last year you reported that an increased emphasis on clinical research could be expected to continue. At the same time, it was reported that the traditional emphasis on basic research would continue. What proportion of your research is clinical?

Answer: Clinical investigations have recently increased, with the result that approximately one-third of our extramural research support relates to clinical studies.

Question: What do you think the right proportion should be?

Answer: There is probably no "right" proportion for clinical research, that would consistently be appropriate. Rather, circumstances dictate the necessary level of support. The program management and planning activities in place at the NIDR make it possible for the Institute to predict and effect changes in emphasis as new basic science discoveries with impact on the prevention, diagnoses, and treatment of disease reach the stage of clinical testing. The current balance of nearly one-third of the funds provided for clinical studies should assure that the mission of near-term improvement in health care and long-term prevention will be forthcoming.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: The current budget constraints affect all areas of the 1983 budget and are not limited to research activities; overhead areas are also experiencing severe budgetary restraints. Economies are being exacted from such administrative areas as travel, supply purchases, and equipment rentals.

Question: What are your most important administrative concerns -- and what are your least important concerns?

Answer: All the Institute's activities are necessary and important; however, those activities associated with grant review and management are given the highest priority. Other administrative concerns, such as supply purchases, travel requests, and equipment purchases are carefully monitored and given the lowest priority.

Question: What criteria do you use for determining your administrative priorities?

Answer: The highest priority goes to those areas where we have a legal requirement such as administering grants and contracts. Secondly, we try to comply with Congressional and Departmental objectives. In all areas, of course, we attempt to perform our tasks in the most efficient and effective manner possible, so there are considerations of cost/benefit ratios.

PREVENTION

Question: What major progress has been made in preventive dental health over the past year?

Answer: Disease prevention is the ultimate aim of NIDR's research efforts. Analysis of our recent National Dental Caries Prevalence Survey has shown that dental caries prevalence in school-aged children has decreased approximately 30 percent since the National Center for Health Statistics survey in 1971-73. This improvement has been attributed to more widespread water fluoridation programs, and to the increased use of fluoride-containing dentifrice, mouthrinses and tablets. Significant progress has also been made in the development of devices that automatically maintain pharmocologically active levels of fluoride near potential sites of disease in the mouth, and in the development of vaccine against caries. In addition, a conference was held in 1981 for educators informing them of the latest dental caries preventive methods. In the area of soft tissue diseases, substantial progress has been made toward the development of safe, effective vaccine against herpesvirus infections. Major progress has also been made in our understanding of the etiology and pathogenesis of periodontal disease and other oral diseases and disorders. These findings should lead to improvement in preventive services in future years.

Question: We understand that significant advances are being made in caries prevention and soft tissues disease. Can you tell us a little about what impact those advances will have on the public?

Answer: As you have indicated, the advances made in caries prevention have resulted in reductions in dental caries prevalence. These reductions mean less pain and discomfort, lower health expenditures and better oral and general health status for the public. The advances that have been made toward the development of a safe, effective vaccine against herpesvirus infections as well as in the treatment of existing herpetic lesions should eventually reduce or prevent much recurrent suffering that a major portion of the population experiences.

PUBLIC INFORMATION PROGRAMS

Question: Do you feel that your public information programs in dental health are having beneficial effects on the older as well as the younger population?

Answer: The NIDR public information programs in dental health are aimed at all ages. Some programs which focus on dental caries are targeted primarily at children and youths who need to be taught preventive methods. Other information programs speak primarily to adults, such as those special population groups undergoing radiation to the head and neck and chemotherapy for cancer or patients with periodontal diseases. This year NIDR provided an exhibit for the White House Conference on Aging, and also contributed to a NIA "Age

Page" leaflet on taking care of teeth. The demand generated for these information programs (including spot radio and TV announcements, films, pamphlets, articles, displays for meetings, posters) has been great and the programs appear to be having a beneficial effect on all populations.

PERIODONTAL DISEASES

Question: Do you already see a trend in reduced periodontal disease as a result of your programs over the past 10 years?

Answer: Research on periodontal diseases over the past 10 years has focused upon improving our understanding of the etiology and pathogenesis of these complex diseases. A few years ago activities in clinical research were expanded through the establishment of three specialized clinical periodontal research centers. Work at these Centers is contributing significantly to our knowledge base as well as to the development of diagnostic and theraputic measures. It is anticipated that as preventive and therapeutic methods evolve further, significant reductions in periodontal diseases will occur.

BUDGET POLICY

Question: What impact do you feel present budget policy could have on your programs over the next three years? How will this affect the public?

Answer: The net result of the 1982 Continuing Resolution will be a slowing of the acquisition of basic and clinical information with a concomitant delay in the development of new and improved preventive and treatment methods.

DIABETES

Question: Research reported from your Institute has shown a link between coxsackieviruses and diabetes in the human. What is the thrust of diabetes research at the Dental Institute?

Answer: The major activities of our diabetes research focus on the role of environmental and genetic factors in the etiology of juvenile-onset diabetes, on studying abnormal tissue responses in the diabetic, and on the reason for the high prevalence of periodontal diseases among juvenile-onset diabetics.

Question: To what extent are you pursuing research on the association between viruses and early-onset diabetes?

Answer: Extensive studies are carried out in our intramural research program on the relationship between viruses and early-onset diabetes in both animals and human. Recently, our investigators have shown for the first time that the development of virus-induced diabetes in mice could be completely prevented by a live attenuated vaccine.

SUBSTITUTE SWEETENERS

Question: As of last year, several sweeteners appeared to be good substitutes for limited use. At the same time, food chemists in Japan were reported to have developed several starch derivatives that, while sweet, may not promote decay. What new advances in the search for substitute sweeteners, which are acceptable to the public and do not promote tooth decay, have been made since last year?

Answer: Several advances have been made:

- Grantees have synthesized an analog of the non-cariogenic sugar substitute, aspartame (recently approved by the FDA), which has increased stability and may, therefore, be usable in a wider variety of manufactured snack foods.
- A controlled epidemiologic survey has just begun to identify the patterns of consumption of specific snack foods by children, and to correlate the results with the incidence of new caries lesions.
- Using a rat feeding system developed in the National Caries Program laboratories, a contractor has begun to investigate the specific components of common snack foods that determine their cariogenic potential in humans.

The latter two studies are essential to determine which foods should be prime candidates for reformulation as further substitute sweeteners are approved for use.

CARIES AND CONSUMER FOOD ITEMS

Question: Last year, you reported that the frequency of eating sugar-containing foods was a more important factor in tooth decay than the amount of sugar consumed. What new initiatives have been taken to inform the public about the decay-causing potential of foods?

Answer: Over the past year, the Dental Institute has continued in its efforts to inform the public about the decay-causing potential of foods. In particular, we have provided information to children and their parents about snacks and dental caries. The materials we produced explain how frequent consumption of sugary snacks increases tooth decay. Alternative snacks are suggested that are tasty and nutritious but do not promote dental caries.

To encourage adolescents who snack between meals to choose non-cariogenic foods, the Institute produced four 60-, 30-, and 10-second radio public service announcements featuring top recording artists. The spot announcements were distributed to 4,000 radio stations nationwide. Also released this year was a 30-second TV public service announcement. This spot also encourages children to enjoy snacks that will not promote tooth decay. According to a recent circulation report, the TV spot was telecast a total of 3,962 times with an estimated viewing audience of 133,396,500 persons.

Both the radio and TV spots encouraged listeners to write to the NIDR for further information on good snacking habits and dental health. To respond to these inquiries the Institute published a pamphlet entitled "Snack Facts." Thus far, we have distributed approximately 150,000 copies of the pamphlet to the general public.

DENTAL MATERIALS

Question: We understand you may be supporting efforts to develop new and less expensive materials to replace the use of gold in dental repair. What progress is being made in the development of more economical dental materials to replace gold?

Answer: The NIDR supports development of less expensive biocompatible alloys for crown and bridge prosthetics. These projects include basic laboratory studies on non-gold alloys containing metals like nickel and chromium and the clinical evaluation of these base metal alloys and possible tissue hypersensitivity to them. At least one of these alloys performs as well as gold alloys and does not cause metal hypersensitivity.

One of the supported projects has recently developed a special method to evaluate compatibility of metals and porcelain. A recent clinical study suggests that special low-gold alloys can serve as viable substitutes for conventional gold casting alloys.

Composite resins, which are now the most popular material for the esthetic restoration of anterior teeth, are also under study as gold alloy substitutes. The durability of special fillers is likely to play a critical role in the clinical longevity of this material, especially when used in posterior teeth. A clinical study of experimental glass-filled material showed very good qualities of durability. This promising experimental material also had superior color stability and marginal durability.

Question: Has there been any progress in the development of so-called biocompatible replacements for teeth?

Answer: The NIDR supports animal research in the use of biocompatible porous titanium implants. This material was found to be successful both as a free standing implant and as an abutment to support a bridge. Its clinical success, firmness in the bone, was explained by the histological finding that bone had filled the porosites of the titanium root. These investigators consider the animal studies with this biocompatible material very encouraging, and plan to begin human studies. Another research team is performing clinical studies of this same material in the shape of a blade implant to determine its efficacy as a support for a complex fixed bridge.

Biocompatible porous high density polyethylene is being tested as a coating for artificial roots in the jaws of animals. These implants will be clinically and histologically evaluated.

WATER FLUORIDATION

Question: Last year you reported that fluoride is the major contributing factor in the National decline in the prevalence of dental caries in school children. Do you still feel that way?

Answer: Our research has shown that dental caries results from the interaction of three factors: oral bacteria that colonize on the tooth surfaces; dietary carbohydrates, like sugars, which are fermented by the oral bacteria into acids that destroy the tooth surfaces; and teeth that are not able to resist the acids formed by the bacteria. There is no evidence that, during the past 7 or 8 years, there has been any change in the normal oral flora or any significant decrease in the consumption of sugars. Therefore, we must conclude that the decline in the prevalence of dental caries in school children as observed in our recent survey is due primarily to the increased use of fluorides, which increases resistance of the teeth.

Fluorides, especially community water fluoridation, continue to be the most effective and least costly public health measure for preventing tooth decay.

DENTAL VACCINES

Question: Last year you reported that, although the practical application of a vaccine to prevent dental caries was quite far off, knowledge of the principles of developing such a vaccine was advancing satisfactorily. Small studies with human volunteers were reported to be encouraging. What significant advances in knowledge can you report?

Answer: The most significant advance in this area was the demonstration of the importance of bacterially produced enzymes of the glucosyltransferase type in regulating bacterial colonization of tooth surfaces. Thus these enzymes have become prime candidates as antigens for immunization against caries.

QUESTIONS SUBMITTED BY SENATOR ANDREWS

DIET AND DENTAL CARIES

Question: The National Caries Program expends substantial funds in a search for "non-cariogenic" artifical sweeteners to replace natural sugars in processed foods. What is the rationale for seeking to develop artifical sweeteners? Natural sugars have physical properties which are important for food processing (for example, use of bulking and preserving agents), not merely the characteristic of providing a sweet taste. If artifical sweeteners do not have those physical properties, who would use the artifical sweeteners and for what purpose would they be used? What evidence does NIDR possess which would indicate that a reduction in sugar consumption in the U.S. would result in a decrease in the incidence of caries?

Answer: Non-sugar sweeteners, both artifical and natural, can be used in a wide variety of foods, especially those foods usually eaten as snacks. Saccharin, cyclamates and the recently approved aspartame, are examples. In Europe, the non-cariogenic sweetener xylitol, has successfully been used to manufacture an array of products including candies, soft drinks, jams and ice cream. When a sweetener provides insufficient bulk, for baking, for example, a metabolically inert bulking substance is used. Several are available and others are being developed by the food industry. There is an abundance of research evidence, collected over several decades in many countries, to demonstrate that a reduction in sugar intake, particularly the frequency of intake, is accompanied by major decreases in caries incidence. The most recent human study was carried out in Finland. Subjects whose foods were sweetened with xylitol developed practically no caries in 18 months in contrast to large caries increments among subjects who ate sugar-sweetened foods.

Question: The National Dental Caries Prevalence Study was released by NIDR in December, 1981. It shows that 37 percent of children in the U.S. under age 17 are caries-free. Ms. Janet Burnelle of the National Caries Program reported to the press that 53 percent of the children living in geographical areas with fluoridated water have no caries. If these statistics are accurate, would it not be more cost-effective to fund efforts to promote the use of fluoride than to persue efforts at diet modification?

Answer: We have not reported data on the percentage of caries-free children in fluoridated areas. However, there is no question that fluoridation of public water supplies is the most cost-effective method of partial prevention of caries and this method is actively promoted by the Centers for Disease Control, PHS. The National Caries Program also promotes the use of self-applied topical fluorides in schools. However, only slightly more than half the population has access to fluoridated water. Furthermore, under the most optimal conditions, fluoride provides only partial protection against caries. To effect major reductions in caries in the entire population it will be necessary to control the causative dietary factors in addition to increasing tooth resistance with fluoride.

Question: Research sponsored by the NIDR - for example that of Dr. Kegeles and Dr. Lund - shows that efforts to modify the human diet and human behavior meet with strong psychological resistance and are ineffective, even when serious illnesses such as diabetes, obesity, cardiac weakness, and respiratory ailments are involved. If this is so, what leads you to believe that the American public would change its eating habits if it could somehow be shown that such behavior modification could lead to a caries decrease?

Answer: Based on previous experience, there appears to be little hope that a large segment of the public will modify their diet to the extent of eliminating sweet snack foods. For that reason, our strategy of caries prevention involves an attempt to provide the consumer with a choice of alternative sweet foods, manufactured with non-cariogenic sweeteners.

Question: NIDR research has shown that caries can result from the consumption of any natural or processed carbohydrate. If that is the case, how can carbohydrate foods be classed as "dangerous" and "non-dangerous" from a standpoint of caries causation?

Answer: Any food substance which is readily fermented to acid by oral bacteria has the potential to cause dental caries. By this criterion, sugars have the highest cariogenic potential, starches substantially less and, for example, sugar-alcohols practically none. The physical form of the food is highly relevant, as sticky foods are available longer for fermentation on the teeth than foods that are rapidly cleared from the mouth. Most critical of all is the frequency with which the fermentable food is eaten.

Question: Recent NIDR contracts have been let in an attempt to measure the "relative cariogenicity" of various foods, yet NIDR research has shown that numerous other factors, such as salivary flow, play a major role in caries causation. If this is so, how can the identification of "relative cariogenicity" be a meaningful concept?

Answer: The NIDR has developed a screening method to assess the cariogenic potential of certain types of foods. The method involves measurements of acid production in humans and caries in laboratory animals, both under normal eating conditions. The results are interpretable only to suggest that under similar conditions of frequency of eating, sequence of foods eaten, fluoride consumption, etc., foods with the highest cariogenic potential index are most likely to initiate dental caries, and are thus the most logical candidates for reformulation with non-cariogenic sweeteners.

Question: Are there significant differences in the dental make-up of rats and human? If so, of what use are attempts at relative cariogenicity testing employing rats?

Answer: There are many differences in the dental make-up of rats and humans and results from animal experiments cannot be directly extrapolated to humans. However, there are many experimental results from rats which have subsequently been confirmed in human trials, studies of fluorides and antimicrobial compounds being good examples. In the numerous instances where ethical considerations preclude human experimentation as, for example, in the assessment of the cariogenic potential of foods, the laboratory animal provides a highly reproducible means of assessing the potential of agents and substances to induce or prevent caries in humans. The situation is analogous to that in which suspected carcinogens are screened in laboratory animals.

Question: The National Health and Nutrition Study (NHANES) supported by the U.S. Public Health Service showed no meaningful relationship between dental disease and sugar consumption, and in fact indicated a negative correlation between dental disease and sugar consumption in the age groups 12 to 17 and 15 to 64. In light of these findings, what dental purpose is to be served by attempting to modify the diet so as to discourage sugar consumption?

Answer: It is not surprising that some survey results, as in the HANES Survey, have not shown a relationship between sugar intake and dental caries. Such surveys have failed to assess the frequency of sugar consumption which is known to be a critical variable. In addition, they have measured the life-long accumulation of caries, rather than the amount of disease that has recently occured. Thus the data compare current dietary habits, with disease that may have been initiated many years earlier. The National Caries Program has recently initiated a survey of diet and caries that will attempt to overcome these methodologic problems.

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

STATEMENT OF DR. LESTER B. SALANS, ACTING DIRECTOR

ACCOMPANIED BY:

DR. THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

L. EARL LAURENCE, EXECUTIVE OFFICER

ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator SCHMITT. The witness is Dr. Lester Salans, Acting Director of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases.

Doctor, I'll be back with you in just about 2 minutes.

[A brief recess was taken.]

Senator SCHMITT. Doctor, would you introduce your colleagues and give us a summary of your statement.

INTRODUCTION OF ASSOCIATES

Dr. SALANS. Thank you, Mr. Chairman.

On my left is Mr. Laurence, Executive Officer. Behind him is Donald Cyphers, our Financial Management Officer, and Dr. Burton, who is our Associate Director for Program Planning and Evaluation.

Senator SCHMITT. I think you're going to need to hold the microphone a little closer.

Dr. SALANS. Thank you.

OPENING REMARKS

Mr. Chairman, with your permission I will submit our full opening statement to you for the record and just highlight some aspects of it.

Senator SCHMITT. Yes.

Dr. SALANS. And I would also like to submit for the record a list of some management initiatives that this Institute has taken in the past several months which we think will enhance the effectiveness and efficiency of the Institute and which may be of interest to the committee.

[The information follows:]

INSTITUTE MANAGEMENT INITIATIVES

During the last several months, the Institute has initiated a number of management initiatives to strengthen and improve the effectiveness of its programs:

Development of a cohesive, working relationship among the Institute's senior staff.

Stronger roles for the Institute's associate directors, in order to achieve greater independence and public visibility for the program clusters.

Identification of research projects that cut across categorical disease areas and are common to more than one program, in order to more closely integrate and coordinate NIADDK support of related research.

Increased interaction between NIADDK's extramural and intramural research programs to broaden the range of expertise that can be brought to bear on the Institute's programs.

Exploration of imaginative organizational approaches that will further enhance the public visibility of the Institute's programs.

Implementation of all remaining facets of the national arthritis plan, the national diabetes plan, and the national digestive diseases plan.

Development of a new system for allocating funds among the Institute's programs.

Improvement of working relationships with professional and lay groups having an interest in NIADDK, through meetings with representatives and elected members of all of NIADDK's major organizations.

Development of a meaningful involvement of NIADDK's National Advisory Council through emphasizing Council's advisory role, and reorganization of Council meetings.

Increased NIADDK involvement with and support of the activities of the National Arthritis Advisory Board, the National Diabetes Advisory Board, and the National Digestive Diseases Advisory Board.

Dr. SALANS. I am very pleased to appear before the committee on behalf of the Institute.

The National Institute of Arthritis, Diabetes, and Digestive Diseases supports and conducts research on many of the most serious diseases affecting the public health. We support much of the clinical research on the diseases of internal medicine, and in related specialties, as well as many basic science disciplines that relate to each of these diseases.

The close interrelationships that exist among our programs and the combination of support for basic and disease-related research has made possible the remarkable scientific productivity and accomplishments of this Institute.

The diseases encompassed by our research programs are among the most life-threatening, debilitating, and costly in the United States, affecting people of every age, sex, and geographic locale.

For example, over 37 million people suffer from the different forms of arthritis. Diabetes affects an estimated 10 million Americans, and is the fifth leading cause of death by disease in this country.

Kidney disease claims the lives of 45,000 Americans each year. And 20 million people suffer from chronic digestive disorders, which claim approximately 200,000 lives each year.

Moreover, the economic burden placed on society by these diseases is enormous, exceeding an estimated $70 billion annually.

Clearly, the responsibility of this Institute for the public health is enormous. This is a responsibility which this Institute is uniquely able to discharge, and which it is pursuing vigorously.

Evidence of this can be seen from the fact that recent research supported by the Institute has produced many significant and exciting scientific advances resulting in unprecedented momentum and opportunities for research which ultimately will lead to improved treatments, cures, and prevention of these diseases.

Since the research advances are so many, let me cite only a few examples of advances limited to those areas that appear in the name of the Institute. We will be happy to submit a more extensive list to you if you'd like.

In the area of arthritis, the quantity and quality of research has increased dramatically, generating portentious new knowledge and opportunities. We now recognize that diseases such as lupus erythematosus and rheumatoid arthritis, previously thought to be single diseases, actually comprise many different subtypes with different causes. For example, some forms of arthritis are clearly related to disturbances of immunologic function. As you have already heard, there has been an explosion in the area of immunologic research, bringing the promise that the immunologic basis and pathogenesis of at least some forms of arthritis can be understood and, perhaps most importantly, that specific effective treatments can be developed.

In diabetes research advances have been remarkable. Not since the discovery of insulin over 60 years ago has the outlook been so promising. As a result of these advances in diabetes research, we are now able, for the first time, to design and undertake a long-term study to address the single most important and controversial clinical question in diabetes: Whether strict control of blood glucose levels and other chemical components of the blood will prevent, postpone, or lessen the severe complications of the disease.

In digestive diseases, Institute-supported scientists have shown that hepatitis B viral DNA can be incorporated into the hereditary mechanisms of the liver cell and that this may be associated with the development of cancer of the liver in patients with chronic hepatitis. Further research might develop methods for clearing the viral infection, that is, for preventing the viral infection in the first place, thereby holding promise for the prevention of this form of cancer.

KIDNEY STONES

Finally, research on kidney stones, which afflict over 1 million Americans, has been so successful that we are now able to prevent recurrences of kidney stones in certain people through treatment regimens using diet and drugs.

Senator SCHMITT. Why do kidney stones appear to be more frequent than just that frequency you mentioned? I just had the impression that kidney stones were more frequent than 1 million in the population.

Dr. SALANS. I think that the data that are available estimate that that is the prevalence. At the moment I'm not sure that that is an accurate reflection of the actual prevalence of the disease, since the data are probably derived primarily from hospitalized patients. Therefore, some people with kidney stones not requiring hospitalization may not be reported.

Senator SCHMITT. Just the number of times that you come in contact with somebody who had a problem with kidney stones seems to be higher than that frequency would suggest.

Dr. SALANS. And kidney stones once formed tend to recur in a large number of these individuals; the estimated recurrence rate is 50 to 80 percent. It is in that very area that the advances have been so successful in recent years, preventing recurrence in people through specific drugs and diets.

Well, it is clear that the Institute is hitting its stride, and it also should be clear that the Institute is committed to continued vigorous support of these and other research programs so that the many opportunities that exist are fully realized.

Mr. Chairman, I'd be happy to answer any questions that you have at this time.

PREPARED STATEMENT

Senator SCHMITT. Your prepared statement will be entered in the record at this point.

[The statement follows:]

STATEMENT OF DR. LESTER B. SALANS

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) supports and conducts research on many of the most serious diseases affecting the public health. We support much of the clinical research on the diseases normally encompassed in the field of internal medicine and related subspecialty fields, as well as many basic science disciplines that span all of the Institute's disease areas. Close, important, and productive interrelationships exist among our programs, with a common thread of research on metabolism and endocrinology running throughout. These interrelationships and the combination of support for basic and disease-related research have made possible and sustain the scientific productivity and accomplishments of this Institute.

The diseases encompassed by our research programs are among the most serious, debilitating and costly in the United States, affecting people of every age, sex, race and geographic locale. The economic burden placed on society by these diseases is enormous, exceeding an estimated $70 billion annually.

Over 37 million people suffer from the different forms of arthritis, including some that are fatal. Diabetes affects an estimated 10 million Americans and is the cause of 33,000 deaths each year among people known to have the disease. When the complications of diabetes are considered, it may be responsible for as many as 300,000 deaths per year. Twenty million Americans suffer from chronic digestive disorders. More Americans are hospitalized because of diseases of the digestive tract than for any other group of diseases and digestive diseases cause approximately 200,000 deaths each year. Although the lives of nearly 10,000 new kidney disease patients are saved by dialysis or kidney transplants each year, kidney disease still claims the lives of 45,000 Americans annually.

Arthritis, Musculoskeletal and Skin Diseases

Arthritis research was the original mandate of this Institute and continues to receive research and programmatic emphasis. A number of significant advances have been made recently in rheumatoid arthritis research. For example, a specific defect in the response of T lymphocytes, a special type of white blood cell that normally suppresses immunoglobulin production, to the Epstein Barr virus has been found in patients with rheumatoid arthritis. This observation may help explain the autoimmune aspects of this disease.

Total lymphoid irradiation (radiation of lymph glands and other lymphoid tissues), a form of X-ray therapy that is highly effective and safe in the treatment of Hodgkin's disease, has now been found to be highly effective in treating rheumatoid arthritis in severely affected patients who do not respond to other forms of treatment.

Retinoic acid, a vitamin A derivative, has been shown to reduce joint inflammation and cartilage destruction in rheumatoid arthritis by inhibiting the production of the enzyme collagenase and reducing levels of prostaglandin

E_2. This research may lead to the development of new drugs that are as effective as corticosteroids, but without their side effects.

In systemic lupus erythematosus (SLE), a serious autoimmune disease that primarily affects women of childbearing age, recent research has uncovered a specific abnormality of estrogen metabolism.

A major advance in the past decade has been the development of artificial joints to replace those destroyed by various forms of arthritis and related diseases. Approximately 120,000 hip replacements and 40,000 knee replacements are performed in the U.S. each year. We are supporting research to improve the durability of implants, and are sponsoring an NIH consensus development conference on total hip replacements in March 1982.

In research on skin diseases, dramatic improvement in the treatment of severe acne has been achieved with the development of 13 cis-retinoic acid, an agent with the capacity to reduce sebum production. In epidermolysis bullosa (EB), a severe blistering disease, research has shown the importance of collagenase in the development of EB, and the promise of the drug diphenylhydantoin, in treatment.

Diabetes, Endocrinology and Metabolic Diseases

Research in diabetes has brought remarkable advances in our understanding and treatment of one of the most serious public health problems in the U.S. today. As a result of recent increased support there is now an unprecedented momentum in diabetes research.

Perhaps one of the most striking research advances is the synthetic production of human insulin, using recombinant DNA techniques. This scientific breakthrough will soon result in unlimited quantities of this hormone for both treatment of diabetics and additional research. These techniques have also permitted the production of human growth hormone for the treatment of growth disorders in children.

There has been new progress in research on transplantation of the insulin-producing cells of the pancreas, the islet cells. Our grantees have transplanted normal islet cells from one animal species into diabetic animals of another species with reversal of the diabetes and without immunologic rejection. They have also identified and neutralized a specific antigen, which may be responsible for the rejection phenomenon. These major achievements may lead to islet cell transplantation in human diabetics.

Major improvements in the day-to-day treatment of diabetes are being made rapidly. New techniques for more reliable monitoring of blood glucose control, and methods that enable diabetics to measure their own blood glucose levels through home monitoring techniques are a great advance for patients. A variety of new automated systems for the delivery of insulin, such as portable and implantable insulin pumps, have been developed by our grantees.

As a result of these and other advances in diabetes research we are now able, for the first time in over 50 years of diabetes research, to design and undertake a long-term study to resolve the single most important and controversial clinical question in diabetes: whether strict control of blood glucose levels will prevent, postpone or lessen the severe complications of the disease.

A major advance in the field of endocrinology is the recent discovery and synthesis of a brain hormone that seems to play a vital role in the body's response to stress. The synthesis of CRF, corticotropin releasing factor, is a powerful new tool in determining exactly how the brain controls the stress response and may eventually lead to new ways to control stress-related diseases, such as peptic ulcers, heart disease, stroke, and sexual dysfunction.

Research on diseases of inborn errors of metabolism is making excellent progress. The biochemical abnormalities in Hunter and Hurler's syndromes, I cell disease, and other mucopolysaccharide storage disorders have been identified. Recent research has also shown that it may be possible to treat inborn errors of metabolism with enzyme replacement therapy.

Although the average life span of cystic fibrosis victims has been extended in the past decade, few cystic fibrosis patients survive into their thirties. Recently, NIADDK-supported research has found that a newly-identified drug, WR2721, may be helpful in treating cystic fibrosis by reducing the viscosity of mucus and enabling cystic fibrosis patients to clear their lungs more effectively. We will continue to support a small-scale clinical trial to capitalize on the encouraging results to date. In Fiscal Year 1983, we also plan to establish a research center for cystic fibrosis in an effort to bring a multidisciplinary approach to the study of this disease.

Digestive Diseases and Nutrition

The recent announcement of the licensing of a vaccine against hepatitis B virus has focused attention on this major world-wide public health problem. In an exciting development, NIADDK-supported scientists have shown that the hepatitis B viral DNA can be incorporated into the nucleus of liver cells and that this may be associated with the development of cancer of the liver. However, this process does not occur during the acute phase of infection, but rather tends to occur between 2 and 8 years later. The implication for designing treatment is to focus on methods to clear the viral infection before that time and thus lower the risk of liver cancer.

The medical treatment of peptic ulcers is generally effective today, because of the development of drugs, such as cimetidine (TAGAMET), that arrest secretion of hydrochloric acid. A new drug, tiotidine, appears to be even more effective than cimetidine.

Nutrition is an area of great public interest and importance. NIADDK now supports five Clinical Nutrition Units that represent a new multidisciplinary approach to nutrition research. We envision that by integrating nutrition activities in medical institutions that support research, training, and patient care, knowledge about specific nutrients and their effect on health, human development, and the prevention and treatment of disease will be generated.

Kidney, Urological and Hematological Diseases

NIADDK supports a wide spectrum of research activities aimed at advancing knowledge about kidney and urologic diseases, so that common and serious diseases such as urinary tract infections, kidney stones and benign prostatic hyperplasia, can be prevented, arrested and treated.

Prevention of the diseases resulting in the enormous human and economic costs of end-stage renal disease (ESRD) is the ultimate goal of our research. At the present time only two of the multiple causes of ESRD, primary hypertension and analgesic-associated nephropathy, are preventable. Glomerulonephritis, which is responsible for over 50 percent of ESRD, is the subject of numerous research projects supported by the NIADDK as well as of two clinical trials aimed at assessing the relative effectiveness of current treatments. Polycystic kidney disease is an inherited disorder responsible for about 10 percent of ESRD. The underlying mechanisms of polycystic kidney disease are being studied in an attempt to determine predisposing factors in the disease so that rational treatment can be devised.

Kidney stones, which afflict over one million Americans, have been the subject of intensive study through the NIADDK-supported Specialized Centers of Research in Urolithiasis. The productivity and success of these centers has been such that recurrences of kidney stones have been prevented in people who form certain types of stones through treatment regimens using diet and drugs.

In a major new finding in sickle cell anemia, NIADDK scientists have been able, for the first time, to actually see the aggregation process of the abnormal blood protein in living red blood cells, the process that causes sickle cell disease. Scientists found that the flexibility of red blood cells, rather than the sickling itself, is the important determinant of red cell destruction and tissue damage in this fatal disease.

Prevention Research

Prevention of disease disability and the severe social, psychological and economic impact of disease through high quality research is a long-standing goal of this Institute. Research on the effects of increased calcium in the diet, particularly after age 40, and regular, moderate exercise as a means of preventing or arresting osteoporosis, an extremely common disease of demineralization or thinning of the bones, is supported by the NIADDK.

In diabetes we have initiated a major clinical trial to resolve the long-standing question of whether strict control of blood glucose levels in insulin-dependent diabetics will prevent, postpone, or lessen the serious complications of diabetes, such as heart disease, stroke, blindness, kidney failure, gangrene and damage to the nervous system.

The Institute is supporting studies of the effects of a high fiber, roughage diet in the prevention of diverticulosis (outpocketings of the inner lining of the large intestine) and its debilitating consequence, diverticulitis, a very common disorder in people over 60 years of age.

A recent large-scale NIADDK study was able to show that recurrent kidney stones may be preventable through drug and diet therapy, a major boon for the estimated one million Americans who suffer from kidney and urinary tract stones.

Research Training

Research training is an area of special emphasis and attention within the NIADDK. The training and development of young people in research, particularly physician scientists who are able to pursue research from the laboratory to the patient's bedside, is essential if we are to realize the many opportunities provided by science today and to maintain this country's leading role in biomedical research. New, young investigators must see science as a viable and stable career field if we are to attract and keep productive people who will be able to pursue research over the extended period of time required to generate significant new knowledge.

In conclusion, Mr. Chairman and Members of the Committee, the budget request for the Institute for 1983 is $379,422,000. I shall be happy to answer questions at this time.

BIOGRAPHICAL SKETCH

NAME: Lester B. Salans, M.D.

POSITION: Acting Director, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases

EDUCATION: B.A., University of Michigan, 1957
M.D., University of Illinois, College of Medicine, 1961

EXPERIENCE:
Acting Director, NIADDK, 1981-present
Associate Director, Diabetes, Endocrinology and Metabolic Diseases, 1976-present
Chief, Cellular Metabolism and Obesity Laboratory, NIADDK, 1977-present
Professor Adjunct, Dartmouth Medical School, 1978-present
Associate Professor, Dartmouth Medical School, 1971-1978
Head, Section of Endocrinology and Metabolism, Dartmouth Hitchcock Medical Center, 1968-1976
Chief Medical Resident, The Hospital of The Rockefeller University, 1967-1968
Fellow, National Institutes of Health Special Fellowship, The Rockefeller University, 1966
Post-doctoral Fellow in Endocrinology and Metabolism, Stanford University Medical Center, 1964
Internship and Residency Training, Internal Medicine, Stanford University Medical Center, 1961-1964

RESEARCH INTEREST AND EXPERIENCE: Diabetes and obesity, mechanism of insulin action, intermediary metabolism

ASSOCIATION MEMBERSHIPS:

American Society of Clinical Investigation
American Federation for Clinical Research
American Society for Clinical Nutrition
Endocrine Society
American Society for Advancement of Sciences
American Diabetes Association
Fellow, Council on Atherosclerosis, American Heart Association
Sigma Xi
Fellow, American College of Nutrition
New York Academy of Sciences

EDITORIAL BOARDS AND JOURNAL REVIEWS:

American Journal of Physiology
Journal of Clinical Investigation
Metabolism
Journal of Lipid Research
Science
American Journal of Nutrition
Journal of Clinical Endocrinology and Metabolism
Endocrinology
Diabetes

SPECIAL AWARDS, CITATIONS,
OR PUBLICATIONS:

Phi Eta Sigma, University of Michigan, 1954
Alpha Omega Alpha, University of Illinois, College of Medicine, 1959
Mosby Scholarship Awards, University of Illinois, College of Medicine, 1951
M.D., cum laude, University of Illinois, College of Medicine, 1961
Distinguished Public Service Award, Juvenile Diabetes Foundation, 1979
National Institutes of Health, NIH Director's Award, 1980
Senior Executive Service Performance Bonus, 1981
Author of more than 50 publications on diabetes, metabolism, and obesity

CALCIUM METABOLISM

Senator Schmitt. Thank you.

Is there any indication that calcium level is a factor in skin disorders—body calcium?

Dr. Salans. That is a question that has been examined and debated for some time. In certain diseases such as scleroderma, which is a disease that affects the skin, there appears to be an enhancement of calcium deposition. Whether or not the calcium deposits occur secondary to the disease and its destruction of the skin, or whether abnormal calcium metabolism contributes to the disorder is not certain.

There are other skin diseases associated with abnormal calcium metabolism, but I'm not aware of a direct cause and effect relationship between the two. That is something I'd be happy to look into in more detail and provide you with more information if you'd like.

Senator Schmitt. I'd appreciate a brief look at it. In some of my own reading somewhere I've run into some suggestions that it might be a factor, for example, in hair loss and in other types of things.

Dr. Salans. Disorders of calcium in the blood and calcium metabolism are very frequent in the population and often coincide with other diseases, not only of the skin but in other tissues and organs. In some instances cause and effect can be demonstrated, but in this case I'm not aware of such a relationship.

Senator Schmitt. We noted in our space flight activity that in certain individuals, not all, a long period of weightlessness did result in calcium loss in the skeletal structure. Others it did not appear to affect. So, obviously, there is a great deal of individuality in the calcium area.

Dr. Salans. Yes.

[The information follows:]

Skin Disease and Calcium

In general, there is no cause and effect relationship between known skin disorders and blood and tissue calcium levels. In longstanding scleroderma, a disease of the connective tissue of the skin, there is a secondary deposition of calcium salts in the skin—but there is no cause and effect relationship between the disease and calcium metabolism. A similar situation pertains in dermatomyositis, particularly in childhood. Pilomatrixoma is another rare skin condition which involves secondary calcium deposition after the disorder has been present for long periods. Also, there is no known relationship between hair loss and blood calcium levels or calcium metabolism.

ARTHRITIS RESEARCH

Senator SCHMITT. Have you found out yet why copper bracelets make my mother's arthritis pain her less? [Laughter.]

I asked that question last year.

Dr. SALANS. Yes; and you can be sure we have spent a lot of time since, looking into it. [Laughter.]

Senator SCHMITT. But still no answer?

Dr. SALANS. There is still no answer as to why it may be helping your mother. There is in the literature some suggestion that some people with arthritis feel better wearing copper bracelets, while others don't. An explanation is lacking. I would suggest that if no harm is induced by wearing a copper bracelet—and that is something we do not as yet know for sure—and as long as wearing the bracelet doesn't keep patients away from their physicians and the medications we know to be effective in the treatment of rheumatoid arthritis, we certainly would not discourage your mother from using her bracelet if she feels better.

Senator SCHMITT. I guess as long as you don't get struck by lightning——

Dr. SALANS. Well, there is an interesting study—I don't remember the details, but it was a study in which they looked at people who wore copper bracelets, weighed the copper bracelets over time, weighed the patient over time, and showed that the weight of the copper bracelet over time decreased, the weight of the patient over time decreased, but the weight of the patient decreased more than did the weight of the copper bracelet. The conclusion of the study as I recall was that there was no explanation for these phenomena and no relationship to the effectiveness of copper bracelets in the treatment of arthritis. [Laughter.]

Senator SCHMITT. That sounds like a geological report. [Laughter.]

Dr. SALANS. The study illustrates the level of scientific sophistication that currently exists in this area.

There are reports that suggest that copper levels may be increased in some patients with rheumatoid arthritis, and that this abnormality may play a role in the development of arthritis. If this is so, and if there is an increased absorption of copper into the system from wearing a copper bracelet, there may be a reason why one would not favor its use. But there is a lack of facts in this area.

REQUEST FOR BUREAU STATUS

Senator SCHMITT. The staff has heard reports that you recommended that your Institute no longer be an Institute but rather be termed a bureau. Is that true? And, if so, what do you have in mind?

Dr. SALANS. Well, we feel——

Senator SCHMITT. Is a bureau bigger or smaller than an institute?

Dr. SALANS. Well, there are three bureaus at the moment at NIH: the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Library of Medicine. The NCI and the NHLBI are the two largest NIH Institutes. We do feel that the Institute is now at the appropriate size for bureau status.

But that isn't the reason why we have asked that the Institute be established as a bureau. We feel that the legislation in 1980—the Health Promotions Act, Public Law 96–538—established in law a variety of responsibilities for the Institute which could most effectively and efficiently be implemented through a bureau with four program divisions: Arthritis, musculoskeletal, and skin diseases; diabetes, endocrinology, and metabolic diseases; digestive diseases and nutrition; and kidney disease, urology, and hematology. The creation of a bureau with divisions for each of our disease program areas will significantly increase the public visibility of each of these areas.

1982 REPROGRAMING

Senator SCHMITT. We have been hearing reports that you may need to have a reprograming request approved. Are those reports accurate in any way? Could you tell us what the problem is, if they are?

Dr. SALANS. Yes, they are, Mr. Chairman. Let me just backtrack one second, if I may, about the bureau status. It is important to point out that if the Institute is converted to bureau from institute status, it will be at no additional cost, either in manpower or resources. [Laughter.]

Now, with regard to reprograming——

Senator SCHMITT. If you believe that, I'll sell you some land on the moon. [Laughter.]

Dr. SALANS. We do plan to request from the committee permission for modest reprograming in 1982. The request for reprograming is a consequence of two things. The language in the continuing resolution for 1982 directs each agency not to reduce any budget account by more than 6 percent below either the House or Senate allowance, whichever is lower. We are now operating at the House level minus 4 percent.

When the Institute follows the 6-percent stipulation, it results in considerable imbalances between our four program clusters, and our programs—imbalances in priority scores, in funding rates, that is, percent of approved grant dollars funded, and great differences among clusters in the size of budget reductions that had to be absorbed.

These imbalances run contrary to a major initiative that we are undertaking in this Institute, which is aimed at achieving greater balance between our clusters and programs and to achieve a more fair and equitable distribution of our funds.

The most important cause for the reprograming request is to attain a more even and equitable distribution amongst our four programs.

The imbalance created by the 6-percent stipulation in the continuing resolution is compounded by another serious budget problem that this Institute faces in 1982. The NIADDK in 1982 is one of only two NIH Institutes that had an actual reduction in its budget from 1981. When this fact is combined with inflation, increased overhead costs, and increased costs of salaries, the negative impact on the Institute is considerable. The degree of imbalance that may have existed between our programs becomes even more magnified under these circumstances.

For these reasons, Mr. Chairman, we plan to submit a request to reprogram a modest portion of our funds in 1982.

PROGRAM BALANCE INITIATIVE

Senator SCHMITT. You use the words "level," "fair," and "equitable." Do you care to pick any one of those or change them? I don't see how you decide on level funding when you just pick the four diseases listed in your title. "Equitable" would be based on the impact on society, I would presume, the difficulty of dealing with that particular disease and not on whether there was an equal amount of money being provided.

Dr. SALANS. The appropriate word is "equitable." By "equitable," we mean that this Institute will allocate funds amongst its programs according to some agreed upon rational, sound, and fair set of principles or criteria. Scientific merit is clearly one, indeed, the most important principle. Therefore, one criterion we will use to allocate funds is the priority score.

It is important to emphasize that we are not, however, aiming for a single pay line across our programs; there will be some degree of difference in priority score pay lines among our clusters and programs, but the magnitude of these discrepancies will be limited and carefully controlled.

A second criterion we will use in the allocation process will be the funding rate, the percent of approved dollars we will actually award to any given cluster or program. For example, it seems inappropriate for us to have one program funding 50 or 60 percent of its approved dollars while another is only funding 5 or 10 percent of its approved dollars.

In addition to these more easily measured parameters, we will be using other factors to make allocation decisions. These will include the public health impact of a disease, the state of the art of research in a given area, special needs and opportunities in a given area of research, and the total size of a program. We will use other criteria as well.

In this way we hope to establish a process which will permit an equitable distribution of our dollars.

We are working together with our colleagues in and outside of the Institute to generate a sound, comprehensible, and equitable process for accomplishing this. We have discussed this with our national advisory council and with our three national advisory boards, and they have given us very valuable advice.

Senator SCHMITT. Is the final decision left to you or to the Director of the Institutes?

Dr. SALANS. In this case the final decision will be in the Office of the Institute Director, but in this Institute the Office of the Director works very closely with the senior staff of the Institute to make those decisions. Let me emphasize that the initial allocation of funds to the clusters made at the beginning of a fiscal year will be based on projections of pay lines and funding rates, for example: Where will a given allocation take each program in terms of priority score? Such projections made at the beginning of the year are only estimates, and therefore, are likely to change.

Senator SCHMITT. Because you don't have the proposals in to award grants.

Dr. SALANS. That's right. The important thing for me to emphasize is that we will be updating our estimates throughout the year, which may result in modest changes in our budget allocations among clusters and programs.

ARTHRITIS RESEARCH

Senator SCHMITT. What do you see on the horizon for the prevention of arthritis?

Dr. SALANS. Mr. Chairman, arthritis is an inflammation of the joints which has many, mostly unknown etiologies or causes. A lot is being done to prevent disability from arthritis, to minimize the crippling effects of these diseases, and to increase the quality of life of those who suffer from arthritis. But, in order to prevent arthritis from occurring in the first place, it is necessary to understand better than we do now the underlying causes of the diseases and the pathogenetic mechanisms through which destruction of the joints and other tissues occurs. Only when the causes and pathogenesis of arthritis are understood can we develop specific interventions to prevent these diseases from occurring. For example, when we understand the immunologic basis of some forms of arthritis we should be able to develop specific therapies to prevent their expression. Some forms of arthritis may be associated with infectious agents. When we identify the infectious agent and determine how it produces arthritis, we can apply specific preventive therapies. At present, for the most part, prevention in arthritis is primarily aimed at preventing disability. This in itself is a considerable goal and significant achievement when it can be effected.

Senator SCHMITT. Is it true that there are periods of remission in certain arthritis patients?

Dr. SALANS. Yes.

Senator SCHMITT. Are those explainable? Do they occur without treatment?

Dr. SALANS. Yes, they can occur spontaneously without treatment. Generally, however, treatment hastens the appearance of remission and prolongs it once it occurs. With specific therapeutic agents, remission can be induced for very long periods of time. The explanation for why the disease goes into remission is not clear. Activation of some forms of arthritis is associated with the appearance in the blood of abnormal antibodies or antigen-antibody "immune complexes" indicative of some abnormality in the body's immune system. Remission in these patients is frequently associated with a disappearance from the blood of these abnormal immune factors. On the other hand, remission can occur even when these abnormal immunologic materials persist in the circulation.

ARTIFICIAL PANCREAS DEVELOPMENT

Senator SCHMITT. What is your assessment of the progress in the various programs designed to develop an artificial pancreas?

Dr. SALANS. There has been considerable progress in one aspect of the program, specifically in the development of automated insulin delivery systems or insulin pumps. These systems, one of which has been developed in your own State at the University of New Mexico by leading researchers in the field, have enabled some diabetic patients to achieve better control of the concentration of blood glucose and other metabolic factors in their blood than heretofore possible.

I should hasten to add that it is generally agreed that this form of therapy is still in an experimental stage—it is not ready for general clinical application, and should only be employed under carefully controlled conditions. In spite of this, approximately 75 to 80 percent of insulin pumps in use in this country are used by individuals who are not under research protocols and who are not being treated in research centers.

And, as you are aware, there have been recent reports of some problems with the insulin pumps—12 deaths have been reported among pump users. These deaths were not due to the pumps themselves but, in most cases, to low blood sugar or hypoglycemia induced by excessive administration of insulin. The same can occur, of course, if too much insulin is administered by conventional treatment, that is, insulin injection.

This is one of the risks that accompanies the uncontrolled use of the insulin pump. It is clear that while this new technology offers the potential for a significant advance, more research is needed before it will be ready for general clinical application.

The development of a true "artificial pancreas," which combines an insulin delivery system with a glucose sensor system, a system that senses the concentration of glucose in the blood and then relays a message to the delivery system to deliver a precise amount of insulin, has been hampered for lack of a reliable, miniaturized glucose sensor system. Little progress has been made in this area to date. Last year the Institute tried to stimulate interest in this area by bringing together in a conference experts from a variety of different disciplines who have been actively involved in this area of research. It is too early to tell whether we have stimulated any interest or progess.

Senator SCHMITT. The implanted pump between the Sandia Laboratories and the University of New Mexico is, I'm happy to report, moving better this year in terms of funding, potential funding, than it was at this time last year.

Dr. SALANS. We are pleased to know that.

Senator SCHMITT. They have just committed to their second implantation, and that is purely an experimental program. There are no patients that I am aware of with the implanted pancreas.

And the first patient has done very well with this last—I guess now almost 2 years.

They are also, I guess, implanting in a number of dogs, special dogs that have no insulin production, I guess—is that correct?

Dr. SALANS. Yes; there are several ways of bringing that state about in dogs.

Senator SCHMITT. And it looks as if there is increasing private sector interest now in the commercialization of the technology. So all of that is moving better than I thought it would a year ago. I'm sure there is still more progress to be made in the financing of this effort.

I am told, as you indicated, that maybe one of the greatest values of this kind of work is understanding better the effect of insulin sequencing within the total body protocol, if I may use the word, and that not only are we developing a potential artificial pancreas but learning more about how to treat the disease of diabetes.

Dr. SALANS. Yes, sir.

SUBMITTED QUESTIONS

Senator SCHMITT. We will have some more questions for the record.

I want to thank all of you, and Dr. Malone again, for sticking with us, for your information and attention, and we would hope that the answers to the questions for the record can be returned to us at the time you correct the hearing transcript.

[The following questions were not asked at the hearing but were submitted for response for the record:]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

BUDGET POLICY

Question: The budget proposes to cap indirect costs for research grants at 90% of actual cost and also to reduce the average cost on non-competing continuation grants by 3 to 4 percent; and to maintain training allowances slightly below the fiscal year 1982 level. What will these policies do to your research and training efforts?

Answer: Adoption of this strategy will enable the Institute to support 158 more research project grants and 101 more trainees than would have been possible without these reductions.

Question: What will it do to the ability of grant recipients to produce good science and good researchers?

Answer: The 3 to 4 percent reduction can be absorbed on a short- term basis but has to have a direct impact on the research which will be conducted if continued. The effect of the reduction in indirect costs, while not having a direct impact on the research projects we support, will have an impact on the universities but we are, as yet, unsure of the real implications. The reduction in training allowances while enabling support of additional trainees, will mean that each training experience will be less than optimally effective and possibly discourage some individuals who had been planning future careers in research.

IMPACT OF CONTINUING RESOLUTION

Question: What has been the impact of the 1982 Continuing Resolution which imposed the lower of the House or the Senate figures?

Answer: The House allowance provided only for additional funds to increase training allowances for the same number of trainees originally requested and the same number of competing research grants as was requested. Since we are also required to absorb the entire October 1981 pay raise, we anticipate a significant reduction in the size of our intramural research program both here in Bethesda, Maryland and our field station in Phoenix, Arizona.

Question: What has been the impact of a 4% reduction beyond that?

Answer: Because of the 4% reduction, each competing research project grant will be reduced by that percentage which precludes our having to reduce the number of projects supported. Research centers will be reduced somewhat more while in research and development contracts, planned new starts will be eliminated and continuing projects will be negotiated at minimally acceptable levels.

IMPACT OF BUDGET

Question: What has been the impact of the cut in your Institute's budget for FY 1982 relative to the FY 1981 level:

Answer: This Institute is one of only two research Institutes at the National Institutes of Health which has a Continuing Resolution that is lower than the 1981 level. The major impact will fall on research project grants.

Question: When was the last time the number of new and competing research grants were as low as they will be in FY 1983?

Answer: Not since 1976 when we awarded 447 competing and new research grants has our level of support been as low and that was before the major initiatives resulting from the recommendations of the three national commissions on arthritis, diabetes and digestive diseases.

Question: If the budget is adopted, what opportunities for research advances will we not be able to take full advantage of?

Answer: Over the past several years the Institute has generated significant discoveries and opportunities for future research. The following are only a few examples of the many opportunities that exist for research in this Institute which will be affected by the 1982 and 1983 budgets.

NIADDK supported research has produced two exciting new findings in rheumatoid arthritis: the discovery of a specific defect in T lymphocytes, a special type of white blood cell that normally suppresses immunoglobulin production in patients with rheumatoid arthritis; and the finding that total lymphoid irradiation, a form of X-ray therapy that is used in the treatment of Hodgkins disease, is highly effective in the treatment of rheumatoid arthritis patients who do not respond to other forms of treatment. The Institute will not be able to pursue these promising leads.

NIADDK supported research has generated new and promising opportunities to define the genetic, immunologic and viral factors in insulin-dependent diabetes and the endocrinologic and metabolic and nutritional aspects of non-insulin dependent diabetes. Under the 1982 and 1983 budgets, fewer investigator-initiated research grants related to the prevention or management of diabetes and its serious complications will be supported in this area.

Recent years have seen an explosion of new information on fundamental aspects of hormone synthesis, secretion and action, and on the metabolic processes that regulate all bodily functions. The ability of the Institute, through support of investigator-initiated research, to take full advantage of the opportunities to translate this into research directly affecting some of the most common and serious diseases of man will be limited.

NIADDK supported research has very recently demonstrated that hepatitis B viral DNA is incorporated into the liver cells of certain patients with chronic active hepatitis, thus putting them at increased risk for developing liver cancer. Additional research may provide an opportunity to prevent the development of liver cancer since the incorporation of viral DNA occurs between 2 and 8 years after the acute phase of the infection. The Institute will not be able to support a proposed clinical trial in this area under the 1982 and 1983 budgets.

The costs of end-stage renal disease are escalating every year. The Institute's ability to support research on the underlying causes of kidney diseases that lead to deterioration of renal function and end-stage renal disease will be restricted.

BUDGET

Question: How will the proposed budget affect your program planning for the coming year? Where will you place your priorities?

Answer: We will continue to maintain emphasis on investigator-initiated, individual research grants (the "R01" type), but we will also endeavor to sustain our other mechanisms of support including intramural research.

Question: How have your research and educational priorities changed as a result of budgetary restrictions and the effects of inflation?

Answer: Qualitatively, they have not changed. We are continuing to maintain a fair balance between our ten categorical programs and the 4 program clusters into which they are organized. Simultaneously we try to maintain stability in the balance between our various mechanisms of award even though inflation will and does impact on them quantitatively.

RUMORED REPROGRAMMING

Question: We are hearing reports about a possible plan by your Institute to request a reprogramming in order to revise your Congressionally approved budget. Under your proposal--who would gain and who would lose?

Answer: The reprogramming proposal has been discussed carefully and extensively with representatives of the various outside constituencies interested in NIADDK's disease areas, and there was a consensus and agreement for the proposed, modest reprogramming.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in Fiscal 1983?

Answer: The President's budget estimate for FY 1983 for NIADDK is $379.4 million. Of this, approximately $14 million are for administrative costs. This is an extremely low rate of expenditure for responsible and effective administrative stewardship and represents the end product of previous cutbacks on the part of the Institute. Nevertheless, we will continue to assess all administrative areas and activities in our endeavor to effect additional savings.

Question: What are your most important administrative concerns--and what are your least important concerns?

Answer: Our most important concern is the proper stewardship of Federal funds and the stability of our intramural research program.

Question: What criteria do you use for determining your administrative priorities?

Answer: Our basic criteria focus on the effective management of our grant and contract programs--from initial review of applications through the life of the funded project.

RESEARCH CENTERS

Question: How much are you spending on research centers in Fiscal 1982--and how much will you spend in Fiscal 1983?

Answer: We estimate an expenditure of $23,401,000 for centers in FY 1982 and $27,393,000 for FY 1983.

This increase from FY 82 to 83 represents the addition of only one new research center, a Cystic Fibrosis Center at a cost of approximately $1 million. The additional increase above 1982 is due to a shift of four existing program project grants to the centers mechanism to reflect more accurately the actual activities in these four programs, plus a modest inflationary increase for centers already existing.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: The figure for FY 1983 represents a carefully considered estimate for centers consistent with NIADDK's budgetary constraints; in our judgment, a reduction in this figure would impinge negatively on essential research and treatment activities.

ARTHRITIS

Question: Please tell us what progress you are making against arthritis in general and juvenile arthritis in particular.

Answer: In general, our knowledge in arthritis and related rheumatic diseases is growing and becoming more precise. This is extremely important because we are talking about a group of about 100 distinct disorders--most with as yet unknown causation. Rheumatoid arthritis (and the related disease lupus erythematosus) formerly thought to be single diseases are now known to comprise multiple, different types due to different causative factors such as genetic predisposition and abnormal and self-destructive immune reactions, possibly combined with environmental triggering factors such as viruses. The research we are supporting has begun to characterize each sub-type in detail with a promise of development of specific, effective treatments.

Particularly important are advances in immunology which are currently taking place at an almost explosive rate; they bear the promise of clarification of the immunologic basis or pathogenesis of some forms of rheumatic diseases.

A concrete example of a research advance in arthritis is represented by the newly-introduced use of total lymphoid irradiation (TLI) for severe rheumatoid arthritis resistant to other conventional therapies. TLI suppresses white blood cells including, probably, specific subsets responsible for the pathogenic process in RA. This is a promising new direction; but we hope we can develop even more specific, effective immunosuppressive therapy aimed at the specific types of lymphocytes pathogenetically active in RA.

We are making constant progress in another area of treatment--that of joint replacement. The use of artificial joints to prevent partial or total disability of patients with long-term, crippling arthritis has gradually become a routine and effective treatment modality.

There is continuous progress with new prostheses being developed for joints other than hips and knees (elbows, shoulders, fingers). The durability of these devices is improving, as we are developing new ways of implantation and fastening of these artificial joints and as we improve their resistance to wear and tear.

With respect to juvenile arthritis--this Institute has let a consortium contract to Baylor University in Texas through which a multicenter study has been organized to study the efficacy of treatment of juvenile arthritis with 2 agents that appear promising on the basis of their performance in certain groups with adult rheumatoid arthritis--D-penicillamine and hydroxychloroquine. The studies have been initiated relatively recently and it is therefore too early to venture predictions concerning treatment outcomes.

DIABETES

Question: What are the major areas of continued research and development in the diabetes field?

Answer: Research in diabetes is being carried out simultaneously along an extremely broad and varied front. There are major efforts to elucidate the precise causes of the two major types of diabetes (insulin-dependent and non-insulin requiring), and to clarify the additional roles played by other related factors be they "environmental" (viral infection, overweight/diet, and others), genetic factors or predispositions, age and others. The search for the precise, causative mechanisms of diabetes is essential for the development of rational, effective therapy and indispensible for the eventual prevention of the disease. A natural corollary to these studies in causation are studies in the basic disciplines immediately related to diabetes--such as endocrinology, metabolism and nutrition.

Another series of studies addresses itself to the hormone, insulin, which is central to normal functioning of the body and to diabetes. These studies are elucidating how insulin is synthesized, secreted, and acts to control many body functions. Other studies are addressed to the precise mechanisms by which circulating insulin affects metabolic activities inside body cells; such studies involve the so-called insulin receptors on the outer cell surface and the way in which insulin and their specific receptors interact and how this interaction, in turn, affects various metabolic mechanisms within the cell.

Still other studies are addressed to improvement of techniques by which insulin-producing pancreatic islet cells can be transplanted from normal animals to diabetic animals in order to perpetuate themselves in the new host and produce the insulin which he requires.

Another major research effort is devoted to the development of improved treatment methods for diabetes in order to minimize the morbidity, disability and mortality of today's patients.

Question: How soon before these advances will impact on improved medical practice for diabetics or is it already having an impact?

Answer: These efforts have already resulted in significant impacts; for instance, perinatal deaths have been cut in half in recent years through the use of improved methods of blood sugar level control.

Question: Can you explain the measurable economic and other benefits to be derived from the developments in diabetes research?

Answer: One immediate goal of an extremely important clinical trial in diabetes which we are initiating now, is a clarification whether precise, "tight" control of blood sugar levels in patients with Type I (insulin-dependent) diabetes can prevent, ameliorate, or postpone the emergence of the severe, long-term disabling and fatal complications of diabetes. The estimated, current annual cost to the Nation of diabetes is $7.4 billion. A major portion of this cost reflects expenditures for medical services and loss of productivity due to these complications. A successful conclusion of the planned clinical trial can provide a potential of preventing or postponing these complications. If it is possible to achieve a 50% reduction of the expected incidence of diabetic complications, the attendant, yearly saving would lie between $3.0 and $3.7 billion.

ARTIFICIAL PANCREAS

Question: What progress has been made in the last year in the use of the insulin infusion system?

Answer: There has been continuous progress in the design, development, and use of the different insulin-infusion pumps during the last few years--especially since NIADDK launched an organized and concerted research and development effort in this field. We solved the problem of internal clogging of these pumps due to previously uncontrollable, inadvertent, precipitation of solids from the insulin solutions. In addition, the newer pumps have improvements in design and reliability based on past experience.

Question: How soon can we expect to see this system in general use?

Answer: We would like to emphasize that these insulin infusion pumps are not meant to represent a new type of general, routine treatment for patients with insulin-requiring diabetes. These pumps are sophisticated tools for experimental use in the study of diabetes. They permit us to improve to a very significant extent blood sugar level control in the patient throughout the day to a degree which is difficult or even impossible to reach with conventional insulin injections.

Question: What evidence is available that this system might diminish the many complications of diabetes?

Answer: These programmable, automated insulin pumps have made it possible to observe selected groups of diabetic patients both in hospital and home settings for prolonged study periods during which their blood sugar levels are close to normal to a degree not possible heretofore.

Using these devices, scientists have demonstrated that strict blood sugar control (a) can improve previously-impaired motor nerve conduction in certain patients with Type II (maturity onset) diabetes, (b) is associated with normalization of previously depressed somatomedins--increasing the growth velocity of young patients with Type I diabetes, and (c) may lead to significant reductions of total blood cholesterol and blood lipid fractions implicated in the early development of atherosclerosis.

VASCULAR COMPLICATIONS OF DIABETES

Question: What is the status of the controlled clinical trials to assess whether and to what extent "strict" control of blood glucose may minimize vascular complications of diabetes?

Answer: We are just embarking on the first phase of this clinical trial. During this period of 6-12 months, a limited feasibility study will be planned. During a subsequent phase, this study will be implemented. These 2 preliminary phases are absolutely essential before a large-scale trial can be initiated. Results of this pilot study will show whether a costly, large-scale study involving many different centers and patients can indeed provide clear cut answers to the basic question--to what extent precise or strict control of blood glucose can minimize the long-term complications of diabetes.

Question: How would this compare with the more traditional approach of periodic injections of insulin?

Answer: In the traditional approach of maintenance treatment for insulin-requiring diabetic patients, the patient injected himself once a day (or sometimes twice) with a mixture of long-acting and short-acting forms of insulin. In theory, this provided him with enough insulin to metabolize in a more or less normal fashion the foods he ingested throughout the day. This system, however, is far from satisfactory because it was not responsive at any one particular time to the precise requirements of the moment for insulin. Once the injection had taken place, a certain amount of insulin was released from the site of the injection into the circulation, but even that release was not necessarily at an even, predictable rate. Thus, throughout the day, the patient was likely to not have enough insulin available at times of peak demand (during and right after meals); he was also likely to perhaps have too much insulin available at night and toward early morning after a prolonged period without meals, and thus may be "hypoglycemic" (have too low a blood sugar level) at that time. Moreover, even if the patient utilized a meal plan which was adjusted to his particular insulin schedule (and vice versa) a variation in daily, physical exercise would lead to periods of fluctuation in his blood sugar level since his insulin supply depended on the amount he had injected and thus did not vary in accordance with the body's physical activity.

DIABETES COORDINATION

Question: This Commitee has been most concerned about careful coordination among all of the NIH Institutes investigating diabetes, so as to assure that the best results are achieved. What steps are being taken to assure such coordination?

Answer: We have established the NIH Diabetes Coordinating Committee to coordinate activities, exchange information, develop policies, engage in joint planning and assess progress. The Committee is headed by the NIADDK Associate Director for Diabetes, Endocrinology, and Metabolic Diseases and is composed of representatives of all Bureaus, Institutes, and Divisions at NIH which have an active role in diabetes activities.

We have also established a Diabetes Mellitus Interagency Coordinating Committee. The NIADDK Associate Director for Diabetes, Endocrinology and Metabolic Diseases serves as Chairman. The members are representatives from selected Institutes within the NIH that are active in diabetes, the Chief Medical Director of the Veterans Administration, a medical officer from the Department of Defense, and representatives of those other Federal departments and agencies whose programs involve diabetes. Through this Committee, we can coordinate activities, avoid overlaps, arrange for joint planning or action steps and determine progress. These coordinating committees have been most effective in avoiding any possibility of overlap or duplication. Their members not only share and discuss ongoing, diabetes-related research activities, but compare plans for future activities and discuss promising directions for future research, obviating situations conducive to duplication or overlap.

CYSTIC FIBROSIS

Question: Last year, you were encouraged to proceed with the establishment of a cystic fibrosis research center to aid the effort against this tragic disease. Can you tell us what has been done?

Answer: I am pleased to inform you that such a center will indeed be established. Our support for its activities will approach $1 million per year. The center will be established at Case-Western Reserve University in Cleveland, Ohio under the leadership of Dr. Carl Doershuk, and we hope that this undertaking will go far in improving the state of the art in this serious disease.

Question: What are your research priorities for CF?

Answer: It is of the utmost importance for us to elucidate precisely the cause or causes and pathologic mechanisms which underlie the disease. Without that, we cannot develop rational therapy which counteracts the basic causes. While this search goes on two specific goals have very high priority. CF is an inherited disease; the offspring of two parents, both heterozygous for CF, has a 25 perent chance of becoming a homozygous CF patient with the disease. It is therefore obvious that a test to identify heterozygous carriers of CF is extremely important in the prevention of CF. Equally important is a practical test for prenatal diagnosis of CF in a pregnant mother known to be at risk. Such a test can reassure the parents that the fetus will be free of the disease in 75% of these pregnancies or can warn them a considerable time prior to its birth that the baby will indeed have CF.

COMPETING CONSTITUENCIES

Question: In an Institute with so many diverse disease responsibilities, it would not be surprising if different programs, or outside constituencies, would pull in different directions. How do you deal with such a problem, should it exist, and have you done anything specific along these lines?

Answer: We have worked hard toward a true unification of NIADDK. We are invoking the following management initiatives:

- Development of a cohesive, working relationship among the Institute's senior staff.
- Stronger roles for the Institute's Associate Directors, in order to achieve greater independence and public visibility for the program clusters.
- Identification of research projects that cut across categorical disease areas and are common to more than one program, in order to more closely integrate and coordinate NIADDK support of related research.
- Increased interaction between NIADDK's Extramural and Intramural research programs to broaden the range of expertise that can be brought to bear on the Institute's programs.
- Exploration of imaginative organizational approaches that will further enhance the public visibility of the Institute's programs.
- Implementation of all remaining facets of the National Arthritis Plan, the National Diabetes Plan and the National Digestive Diseases Plan.
- Development of a new system for allocating funds among the Institute's programs.
- Improvement of working relationships with professional and lay groups having an interest in NIADDK, through meetings with representatives and elected members of all of NIADDK's major organizations.

Question: What kind of criteria do you use to allocate research grant dollars among your 10 different programs in FY 1982 and FY 1983, and does the research community feel comfortable with these?

Answer: We are embarking on a new approach to the allocation of our funds to the various programs of NIADDK. The primary emphasis of our budget allocation is budgeting according to program clusters (arthritis, musculoskeletal and skin diseases; diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic and blood diseases). This permits each Associate Director a greater degree of flexibility for budgeting among individual programs within a cluster. Initial allocation of increases or decreases of funds appropriated to the Institute are based on an agreed upon set of guiding principles. These include scientific merit as determined by priority score paylines and award rates. Discrepancies in paylines between clusters and programs would not be greater than a certain range of points; discrepancies between clusters and programs in the percentage of approved grants that are funded ("award rates") would be minimized and kept at a low level. A "window" delineated by the two principles above would provide a fair allocation action. Other modifying factors: special opportunities or needs, the magnitude of the health problem, and Congressional/administration directives. A small reserve of each cluster's budget would also be utilized to modulate the allocation process. These principles and plans have been presented broadly to representatives of the various scientific and professional constituencies of NIADDK and they feel comfortable with them.

TRAINING

Question: In last year's hearings, NIADDK indicated a drop in the number of clinical investigators participating in the Institute's training programs and identified some of the factors contributing to the decline. Where do matters presently stand?

Answer: Basically, there has been no great change in the situation . Due to current economic conditions, difficult choices have to be made in developing the budget for 1983. We anticipate training fewer clinical investigators than in past years.

Question: What funds have been set aside for the training of the next generation of research professionals in the field?

Answer: Since NIADDK pursues its mission on a budget year to budget year basis, it cannot set aside any possible surplus funds for future use for the training of the next generation of research professionals. The amounts included in the budget for research training is $17,949,000 in 1982 and $19,135,000 in 1983.

Question: How can more individuals be encouraged to pursue a career in the ten research areas for which the Institute is responsible?

Answer: Like the other Institutes at NIH, NIADDK depends to a large extent on the specific attraction of the individual, young physician to biomedical research (rather than to practice). This basic orientation in the individual is absolutely essential in assuring that sufficient, well-trained research workers will pursue a career in any 1 of the 10 program areas of NIADDK. Clearly, the economic rewards of the practice of medicine are so much greater than the remuneration for biomedical research that this basic attraction to research is an absolute prerequisite for the pursuit of a biomedical research career. NIADDK has initiated a program for predoctoral, short-term research training awards to encourage medical students into brief (usually between terms) exposure to research activities. In addition, we have supported an upward revision of stipends in fellowships and training grants and have developed new career-supporting, advanced training awards, particularly in areas of special need. Thus, in addition to individual fellowships and institutional training grants, NIADDK funds research career development awards, clinical investigator awards, and new investigator research awards, all tailored to the individual requirements of a variety of young clinicians preparing to pursue a career in research.

Question: What non-federal or non-governmental sources of funding could be tapped to expand the pool of researchers?

Answer: We believe that the voluntary health organizations concerned with this Institute are already supplementing NIH's support of research and research training to a near maximum of their ability.

INSULIN AND HUMAN GROWTH HORMONE

Question: To what extent are you involved in clinical trials using insulin produced by recombinant DNA methods?

Answer: Grantees of this Institute laid the foundation with their experimental work for the eventual, successful production of insulin and human growth hormone by recombinant DNA methods.

Question: Are you also involved in clinical trials using genetically engineered human growth hormone and, if so, with what results?

Answer: The Institute is not involved directly in ongoing, clinical trials which evaluate these man-made hormones--though some present and past grantees, because of their experience with human growth hormone, are participating in this assessment. Based on results obtained to date, both synthetic hormones appear to be safe and clinically effective.

TREATMENT OF KIDNEY DISEASE

Question: What are the latest developments in the area of renal disease?

Answer: In general, transplantation of a donor kidney from a close, blood relative (parent, child, or sibling) into a patient with irreversible kidney failure can be termed a successful method. In most instances, we can expect that the transplanted graft will remain functional from 5-7 years--giving the patient a fairly normal life and freedom from thrice weekly maintenance dialysis.

Question: How successful are renal transplants at the present time?

Answer: Transplantation of cadaver kidneys from other than close blood relatives has met with only limited success; many grafts are rejected within 1-3 years and the patient, to save his life, must go back on maintenance dialysis. However, we would like to point out a research advance in this area: New research has shown that multiple blood transfusions prior to transplantation enhances the first-year graft survival rate by up to 60%--a significant prevention of early graft failure.

Question: What work do you do on finding ways to help kidney victims improve their restrictive lifestyles?

Answer: Some of the restrictive lifestyles of dialysis patients are conditioned by the side effects of maintenance dialysis--such as the weakness which accompanies anemia, bone pain and occasional fractures which accompany the bone disorders of chronic kidney failure and maintenance dialysis, or weakness in the extremities due to impairment of the peripheral nervous system. Ongoing research is aimed at these complications and their rate has been dropping gradually. Moreover, we have pioneered other types of maintenance dialysis such as home dialysis; overnight, peritoneal machine dialysis; and continuous ambulatory peritoneal dialysis ("CAPD") which tend to lighten the burden of a strict schedule of 3 times weekly, prolonged maintenance dialysis treatments away from the home of the patient. Earlier studies supported by the Institute which resulted in a significant increase in the efficiency of hemodialysis devices and methodology have made it possible to decrease gradually the traditional treatment time of dialysis from 8 hours to 4 hours or less per treatment session. The Institute has also supported development of a miniaturized, artificial kidney which a patient (trained to treat himself) can carry in a suitcase on vacations to carry out dialysis in hotel rooms or recreational vehicles.

HYPERTENSION AND KIDNEY DISEASE

Question: Hypertension frequently contributes to renal disease and can also result from renal insufficiency. Therefore, it would seem to be appropriate for your Institute and the Heart Institute to work together in this area of research. What type of cooperation exists between the two institutes in this area?

Answer: Several years ago, the National Heart, Lung and Blood Institute (NHLBI) had launched a nation-wide program for professional and lay education concerning the long-term dangers of hypertension, including selected population screening programs combined with follow-up treatment efforts. Since one of the possible end results of long-term, untreated hypertension is a type of chronic, progressive kidney disease which frequently results in end-stage renal failure, program staff of NIADDK has followed these efforts closely and with great interest. There are ongoing, formal and informal contacts and exchanges of information relative to hypertension-caused renal arteriolosclerosis with the extramural and intramural staff of NHLBI, particularly since this is one of the few renal disease entities amenable to prevention. Being aware of their commonality of interests, the relevant staffs of both Institutes are making constant efforts at sharing and exchanging information concerning ongoing work and future plans.

MORBID OBESITY

Question: What is new in the treatment of so-called morbid obesity?

Answer: Although a variety of drastic medical treatments has been tried in the treatment of morbid obesity, including prolonged fasting and very low calorie diets consisting principally of protein, only one-third to two-thirds of morbidly obese persons who seek such treatment will remain on these regimens for sufficient periods of time to lose a significant proportion (up to two-thirds) of their excess weight. Of those who are successful in losing a substantial quantity of weight, it is estimated that only about 10-20% are able to maintain the loss for more than a few years.

Question: With the many complications of intestinal bypass surgery for morbid obesity having been identified, should this technique still be promoted and used?

Answer: Intestinal bypass surgery for morbid obesity has been known experimentally for about 15 years and its use has become very widespread as a routine, surgical treatment during the last 7 years.

The most common, serious complications of jejunoileal bypass include a high incidence of oxalate-containing kidney stones, unremitting diarrhea, development of various nutritional deficiencies, including protein malnutrition, and possibly accelerated gallstone formation. Serious kidney problems may also develop. Unless they also receive long-term dietary and behavioral management, a few patients will regain much or all of their lost weight. Other long-term complications include a sometimes fatal liver cirrhosis (probably related to bacterial overgrowth in the excluded intestinal segment), and depletion of fat-soluble vitamins and trace elements, arthritis and metabolic bone disease. Many, but not necessarily all, of these complications can be prevented or mitigated by meticulous follow-up care.

Question: How successful are some of the alternative techniques to bypass surgery?

Answer: Even though intestinal bypass surgery can be effective in reducing morbid obesity, the risks of undesirable side effects were so real that alternative techniques have been developed--primarily during the last 7 years. These include gastric bypass surgery, and gastroplasty ("gastric stapling"). (Other procedures are still in the early stages of development; for instance, the biliopancreatic bypass.) It is generally accepted that gastric bypass and gastroplasty are connected with considerable less risk of untoward side effects than intestinal bypass surgery. A comparison of the different surgical procedures involving the stomach is difficult at present because of constantly changing, surgical techniques and follow-up data of insufficient size and duration--particularly among the more recently developed operations. With respect to the certainty and permanence of weight loss, the outcome of gastric surgery is somewhat less predictable than for the more established and longer known intestinal bypass methods. Some patients learn to circumvent the obstacle of the newly created small gastric food reservoir by constant nibbling or eating of small meals throughout their waking hours.

We would like to emphasize that surgical interventions should be limited to morbidly obese patients with serious physical health or psychosocial problems. Such patients should have given a fair trial (preferably on repeated occasions) to suitable non-surgical treatments such as calorie restriction and behavioral therapy, and failed to improve adequately, or relapsed within a relatively short time after initial periods of successful weight loss.

ARTHRITIS

Question: What have you learned about possible causes of arthritis, particularly viral causes?

Answer: As our knowledge in arthritis increases, it has become progressively clear that there is no single, simple cause for "arthritis", probably not even for osteoarthritis, the degenerative arthritis of advancing age which most of us acquire to some degree or other. In the case of the rheumatic arthritides, knowledge is developing that among causative factors are genetic predisposition and aberrant destructive, immune reactions, possibly triggered by environmental factors including viral infections. Probably more than one specific virus are involved among infectious triggers. Suspect thus far are the Epstein-Barr virus, the Rubella virus and other viral organisms in isolates now being studied at the Montefiore Center (New York), the Waxman Institute (Rutgers) and others.

Question: What can you tell us about the findings reported from London that link the Rubella virus to chronic arthritis?

Answer: There have been reports from London on the isolation of the Rubella virus from patients with rheumatoid arthritis. Similar efforts to isolate Rubella virus from joint fluids and tissue biopsies in the U.S. have not been successful.

Question: To what extent is your Institute involved in studies using x-rays to treat severe rheumatoid arthritis?

Answer: This question refers to total lymphoid irradiation, the use of X-radiation to inactivate, at least for moderate to long periods of time, the lymphatic tissues in the body. This treatment reduces production of specific antibodies implicated in the pathogenesis of rheumatoid arthritis by the body's lymphocytes. Though not a "cure", this treatment promises to be effective in inducing significant remissions of the disease for up to 18 months. Use of this treatment (heretofore routinely used in patients with Hodgkins disease) was pioneered by the Institute grantees in Boston who are continuing to refine this method further.

NATIONAL ARTHRITIS COMMISSION RECOMMENDATIONS

Question: In April 1976, the National Commission on Arthritis and Related Musculoskeletal Diseases submitted its four-volume report to the Congress and the President. Volume I contains the "Arthritis Plan": a blueprint for action to alleviate the problems of arthritis patients. What successes or particular difficulties are you having in implementing any of the recommendations of the National Commission's Report?

Answer: In response to the National Arthritis Plan, the Institute:

1. Created the Office of the Associate Director for Arthritis, Musculoskeletal, and Skin Diseases in 1976.

2. Established the Arthritis Interagency Coordinating Committee in 1976.

3. Initiated the Multipurpose Arthritis Centers Program in 1977, there were 21 such centers geographically dispersed throughout the nation in Fiscal Year 1981.

4. Established the Office of Arthritis Epidemiology and Data Systems in 1977.

5. Created the Arthritis Information Clearinghouse in 1978.

6. Initiated the National Arthritis Advisory Board in 1976 and again in 1981 after its original 3-year Congressional authorization had lapsed.

Concurrently with these actions, there has been an impressive growth in funding in arthritis and musculoskeletal diseases in both the intramural and extramural programs of NIADDK.

On the whole, NIADDK is proud of its successful efforts in furthering the original Arthritis Plan, and it fully intends to continue making maximal efforts in this direction through its own initiative and in consultation and collaboration with the National Arthritis Advisory Board.

HODGEPODGE OR LOGIC?

Question: Your Institute is responsible for many different diseases, and to the uninitiated, it might appear to be a strange mix. Are you really a hodgepodge--or is there logic to the system?

Answer: The Institute's name and its many responsibilities may give the impression of great and arbitray diversity. A close examination of the research fields involved and especially the basic research and the basic biomedical disciplines utilized discloses an unexpected unity of metabolic, immunologic, and physiologic mechanisms. Autoimmunity is the common basis of, or a major factor in, diabetes, rheumatoid arthritis and related rheumatic diseases, inflammatory bowel diseaes, hepatitis and cirrhosis, the glomerulonephritides, and many others.

The precise etiology of Type I diabetes is not yet known. In addition to genetic factors and predispositions, there is the possibility of viral causation or triggering and the probability of an aberrant autoimmune process which results in the destruction of insulin-producing beta cells.

A similar probability of destructive autoimmune reactions exists in rheumatoid arthritis and almost certainly underlies lupus erythematosus. Aberrant immune mechanisms are also suspected in Crohn's disease of the bowel in "chronic, active hepatitis" and in primary billiary cirrhosis. In the different glomerulonephritides, the largest group of renal diseases which leads to end-stage renal disease, the glomerulus is either attacked directly by antibodies or incapacitated by immune complexes which it filters out of the circulation.

Common threads are found between diabetes, endocrinology, metabolism, and nutrition. The dividing line between metabolism and nutrition is indistinct; the same is the case with diabetes, endocrinology, and metabolism which interdigitate. Nutrition and diabetes are closely involved with each other.

Thus despite a great diversity of topics on the surface, the Institute benefits greatly from an advantageous synergism in directly or indirectly interdigitating research efforts.

GENE SPLICING

Question: How will the new advances in "gene splicing" technology be of benefit in the diseases covered by your Institute?

Answer: At the present time, we are witnessing the emerging, commercial production of synthetic, human insulin produced through recombinant DNA technology. The first clinical trials of this material are now being conducted and preliminary indications indicate that the synthetic hormone appears to be both safe and clinically effective. This new source of insulin is of the utmost importance to the many thousands of patients with Type I diabetes who require daily injections of insulin. Availability of the man-made hormone is important to assure a future supply of insulin for an increasing number of patients requiring daily injections. In addition, the fact that it is the human hormone and not porcine or bovine material may prove an advantage in the long run. The human hormone may prove somewhat more efficacious and may prevent immunologic inactivation of animal hormone in some patients.

Similarly, the first quantities of synthetic human growth hormone (HGH) are becoming available and are being tested clinically. Human growth hormone has been the only substance able to prevent tragic hypopituitary dwarfism throughout the world. This Institute, through its National Pituitary Agency, has been able to support research related to HGH and even a major treatment effort among hypopituitary children using natural HGH extracted from human pituitary glands taken from cadavers. The quantities available, however, were insufficient; moreover, practically no HGH was available throughout the rest of the world. The future benefits of an unlimited supply of HGH are obvious. They will even be greater now that recently emerging research results have shown that treatment with HGH of certain sub-sets of normal-variant children with extremely short stature can aid them to attain near-normal height.

These are just 2 concrete examples of future benefits of formerly unavailable peptide hormones. The number of examples will multiply each year as new products are be synthesized--not only hormones but pure and uniform antibodies ("monoclonal antibodies") with potent, therapeutic potential, and many other previously unavailable, beneficial biologicals.

DISEASE PREVENTION

Question: This subcommittee has heard about NIH's emphasis on studies related to disease prevention. To what extent does your Institute have a major stake in this approach?

Answer: NIADDK funds $19 million of studies related to a narrow definition of prevention ("primary prevention"). If we use a broader definition of prevention, which includes prevention of damage, disability and premature death due to a disease, then the figure is $64 million. The following are the most important prevention areas for NIADDK.

Diabetes:

1) A well-controlled, clinical trial to establish whether long-term, "tight" control of blood sugar levels can prevent or ameliorate the serious clinical complications of Type I (insulin-requiring) diabetes.

2) Prevention of Type II (maturity onset) diabetes through avoidance of obesity, physical exercise, diet and appetite regulation.

Osteoporosis

Studies on preventive role of estrogens, high calcium intake, fluoride supplementation, and weight-bearing exercises.

Diverticulosis/Diverticulitis:

These conditions become more prominent with advancing age. Studies deal with the role of dietary fiber in preventing diverticulosis (and thus diverticulitis).

Urinary Tract Stones:

Studies on prevention of recurrence of urinary tract stones in patients who are habitual stone-formers through diagnosis of causative metabolic derangements, such as hypercalcemia, hyperuricemia, and oxaluria, followed by selective drug and diet therapy.

These are just 4 major examples in the 4 major disease areas of the Institute of prevention-related research efforts. Examples in other programs are studies related to the prevention of:

- Permanent life-long facial disfigurement from intractable acne with 13, cis-retinoic acid.
- Dwarfism extreme short stature with human growth hormone.
- Endocrine disorders through hormone replacement or hormone antagonists.
- Metabolic diseases through enzyme replacement.
- Cystic fibrosis--Efforts to develop heterozygote screening tests and prenatal tests.
- Obesity, a factor implicated in Type II diabetes, hypertension/cardiovascular disease, osteoarthritis or gallstones. Studies are focused on regulation of appetite, satiety, hunger, behavior modification, and basic metabolic aberrations.
- Kidney damage and failure through avoidance of abuse of analgesic combinations and exposure to toxic substances.
- Kidney failure through aggressive therapy of primary hypertension.
- Cooley's and Sickle Cell Anemia through effective prenatal tests.

DIGESTIVE DISEASES

Question: Your institute funds a broad area of research in digestive diseases, including diseases of the liver. Could you tell us about your progress in this area?

Answer: There has been progress along a broad front of studies in this area. The following are but 2 landmark examples.

In a particularly sophisticated study, Institute grantees followed a group of patients who had been found infected with Type B hepatitis. A majority of patients recovered from their acute disease. Others became temporary "carriers" of the virus. Still others gradually lapsed into "chronic, active hepatitis" and continued to harbor the Type B hepatitis virus in their liver cells. With the passage of time, these scientists were able to demonstrate that in certain patients of the latter group, the viral DNA (the material which determines all hereditary activities) gradually becomes integrated into components of the hosts' liver cell nucleus. They also found indications in other patients with known liver cancer that viral DNA was incorporated into nuclear material of the liver cells. This work represents an important indication of what could be the natural history of the genesis of primary cancer of the liver, beginning with an acute viral infection which progresses through a "carrier" stage to chronic disease and finally produces a permanent change of the host's hereditary liver apparatus resulting in malignancy.

Another research advance involves the area of liver transplantation. In previous years, liver transplantation has been a less-than-satisfactory experimental procedure to deal with congenital liver abnormalities of the new-born or to replace an organ which had been lost to disease or trauma. The functional survival of newly-grafted organs was usually of a low order and most transplanted livers were rejected between 3 and 12 months. Recently, a new immunosuppressive agent has been utilized in liver transplantation--cyclosporin A. Through the use of cyclosporin A and a significant reduction of a previously used immunosuppressive agent--prednisone--the outcomes of liver transplantation have improved significantly. It is too early to make definite statements at this time, especially since long-term use of cyclosporin A is connected with definite toxic effect on the kidney. The one year survival of liver grafts in the small number of patients maintained thus far with cyclosporin A has increased significantly. Follow-up studies are now being conducted.

SUBCOMMITTEE RECESS

Senator SCHMITT. The subcommittee itself will stand in recess until 10 a.m., Friday, February 26, when we will meet in room 1114 of this building to receive testimony from the Office of the Assistant Secretary for Health.

Thank you very much.

[Whereupon, at 5:15 p.m., Tuesday, February 23, the subcommittee was recessed, to reconvene at 10 a.m., Friday, February 26.]

DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 1983

MONDAY, FEBRUARY 22, 1982

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, D.C.

The subcommittee met at 1:32 p.m. in room 1318, Everett McKinley Dirksen Senate Office Building, Hon. Warren Rudman presiding.

Present: Senators Andrews and Rudman.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

NATIONAL INSTITUTE ON AGING

STATEMENT OF DR. ROBERT N. BUTLER, DIRECTOR

ACCOMPANIED BY:
- **ROBERT RINGLER, DEPUTY DIRECTOR**
- **THOMAS MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH**
- **ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

SUBCOMMITTEE PROCEDURE

Senator RUDMAN. The subcommittee will come to order.

Today, we are going to resume our fiscal 1983 appropriation hearings with witnesses from NIH. NIH, of course, is the Federal Government's principal program for conducting and supporting biomedical research.

In one of the documents submitted to support its fiscal 1983 budget, the administration pointed out that health science research is extremely dependent upon public support, with the Federal Government providing over 60 percent of the necessary funding.

The administration stated that "it is through this continued public support of research that major biomedical advances have occurred so rapidly in the past 25 years."

It is noteworthy that the administration has backed its words with a request that fiscal 1983 funding for NIH be increased by $109 million in a domestic budget noted far more for program reductions than for increases.

On the other hand, NIH does face a major problem; a growing shortage of leaders. It now appears that a dozen key positions, including directorships of six Institutes and the directorship of NIH itself are or will be vacant. In addition, there are vacancies in several important support positions. More on this in just a moment.

Because of scheduling problems, our fiscal 1983 NIH hearings are being held somewhat in reverse order than is usual. We will have another hearing tomorrow morning and again in the afternoon when we will hear the Acting Director's overview plus additional Institutes.

Our first witness will be Dr. Robert M. Butler, Director of the National Institute on Aging, who is reported to be one of those stepping down. We are sorry to learn of your possible departure, Dr. Butler, but we certainly welcome you here today.

NIH APPOINTMENTS

Before getting to your testimony, I want to ask Acting Director Malone about the NIH vacancies. Then, we can proceed from there.

Dr. Malone, we know of 12 major vacancies at NIH. Are there additional ones that we are unaware of?

Dr. MALONE. Mr. Chairman, if you detect a smile on my face, it is due to the fact that today the President announced the nomination of Dr. Wyngaarden as the next Director of the National Institutes of Health.

Senator RUDMAN. We are aware of that. Do you know what the timetable is for him to get into action?

Dr. MALONE. I understand that he will be coming to Washington around March 1. Pending confirmation by the Senate, he should be on board within a matter of weeks.

Senator RUDMAN. How about the other vacancies?

Dr. MALONE. The other vacancies, obviously, depend upon the new Director's arrival. We feel, and the Secretary has felt, that he should have a major say in these appointments. We have established search committees for all the vacancies. Two of them have been completed, and the others are in various stages of progress. I would estimate that by late summer all the vacancies should be filled.

Senator RUDMAN. I would like your candid view of the impact over the past year of the number of unfilled vacancies in top leadership positions in NIH.

Dr. MALONE. I am in a particularly good position to answer that question, Mr. Chairman. When the Secretary asked me if I would serve as Acting Director, I did it knowing full well that the NIH, as a unique agency, has layers of excellence.

We have had a number of people acting, but we have seen very little difference in the activities of the NIH. The acting directors have in many instances performed as well as permanent individuals.

Senator RUDMAN. If this were the New Hampshire Legislature, after that statement, we would immediately abolish all of those other positions. [Laughter.]

Dr. MALONE. No, no; I want Dr. Wyngaarden to come on.

I would also like to say, Mr. Chairman, that the vacancies really represent normal attrition. Some of them involve retirements; some of them involve people who have decided to do other things at NIH after being in the job for 10 years. And, of course, some of them involve better attractions on the outside, particularly in the case of those who have children in college and the Government cannot compete with the attractions in academic institutions and industry.

Senator RUDMAN. As is customary, the Directors of each of the Institutes are going to be with us for the hearings today and tomorrow. This will give members of the subcommittee the opportunity to ask questions of Institute members whose testimony they may have missed.

I think we will have you proceed to summarize your statement.

I want to thank my colleague, Senator Andrews, for joining me here. We sometimes have lonely hearings early in the week.

Senator ANDREWS. I want to assure my colleague I just wanted to find out where the bodies are buried since I have to chair the hearing tomorrow.

Senator RUDMAN. You may proceed to summarize your statement. The entire statement will be in the hearing record.

If you would like to, please introduce your colleagues to us.

INTRODUCTION OF ASSOCIATES

Dr. BUTLER. My name is Dr. Robert N. Butler, Director of the National Institute on Aging.

I will introduce the individuals accompanying me.

To my immediate left is Dr. Robert L. Ringler, Deputy Director of the National Institute on Aging.

Behind him is Mr. David L. Chicchirichi, the Executive Officer of the National Institute on Aging, and Ms. Karyn Ross, Budget Officer of the Institute. Also Mr. Richard Miller, of the Division of Financial Management, NIH, and Anthony Itteilag, Deputy Assistant Secretary of the Budget of the Department of Health and Human Services.

AREAS OF PROGRESS

In the interest of saving time, I would like to submit the full statement for the record and just briefly highlight three important areas of progress made by the Institute.

First, the evolution of geriatric medicine; second, the awesome and destructive problem of senile dementia; and third, research that bears upon health promotion.

GERIATRIC MEDICINE

I would first like to discuss geriatric medicine. In addition to developing new centers of excellence in a significant number of medical schools, we have continued to advance the concept of the teaching nursing home. As you probably know, among health care costs, nursing home costs are the most rapidly escalating.

Nursing homes get 40 percent of Medicaid. We have more patients on any given day in nursing homes than we have in general hospitals. Yet, we know surprisingly little about the characteristics of patients in such institutions and have rare opportunities to undertake important studies that bear upon such chronic ailments as senile dementia, such destructive conditions as incontinence, and other topics that have just not been in the mainstream of contemporary medical thought.

Regarding the second topic, senile dementia of the Alzheimer's type, perhaps one-half of the 1 million people in nursing homes suffer from this condition. For years, it was thought that senility was inevitable with age; that it was not treatable; and that it was probably due to hardening of the arteries. We now know that those particular theories are not totally correct.

More to the point, there have been some exciting findings. One of them bears upon a significant reduction of a particular enzyme in the memory portion of the brain. We are now trying to find some way of remedying that deficiency, with the assumption that the deficiency is an important contribution to the development of the memory disorder.

You may also have noticed over the weekend in the Washington Post an extremely fascinating report of some work by Dr. Stanley Prusner, of the University of California in San Francisco. This work was supported by the National Institute of Neurological and Communicative Disorders and Stroke as well as the National Institute on Aging. The findings relate to unusual substances which can replicate themselves and yet do not appear to have nucleic acids. Nucleic acids are generally thought of as being the significant genetic building block. Its importance relates to its possible role as a slow virus in relation to the development of senile dementia.

Finally, I indicated that I would touch upon health promotion, which is particularly important in the field of aging. We must identify a variety of risk factors that help maintain the effective functioning of older persons. We must know more about exercise physiology, nutritional requirements, and ways of defining functional age.

In brief, these are three areas of some progress in this past year. And I come, Mr. Chairman, to request a fiscal year 1983 budget for the National Institute on Aging of $84,556,000.

Thank you.

AVERAGE LIFESPAN

Senator RUDMAN. Dr. Butler, just several questions that are prompted by recent reports that have come to my attention and members of the staff.

There has been some recent conjecture that it appears like the goal we might reach, at least with the state of the art as it is now, is a lifespan, an average lifespan, of 85 years. That seems to be a number that people speak about quite a bit. Does that seem like a reasonable outlook for the near future in terms of medical science today?

Dr. BUTLER. No; I know that is Dr. James Fries' notion from Stanford University, but I think the distinction has to be made between average lifespan, which is the receivership from some past year such as in the life insurance tables—from birth, May 1965, or the like—and lifespan itself, which is separate from life expectancy. Life expectancy is the maximal inherent natural lifespan of a particular species. Perhaps 100 to 110 is the inherent natural lifespan of human beings.

It is interesting that there is an 85-year projection for average lifespan since the fastest growing age group in the United States currently is the 85-plus age group. The fastest declining mortality rates are also in the 85-plus age group. The fact is, of course, important in terms of nursing home studies because 20 percent of people over 85 are in nursing homes. The vast majority of these people, about 85 percent, are women. So in this country we already have gone beyond that 85-year average age that Dr. Fries speaks about.

Senator RUDMAN. That being so, I expect you will agree there are some very serious and interesting implications for society and for the individuals themselves, if we are talking about lifespans that are now going to span 85 years.

Dr. BUTLER. That is absolutely right. Again, this is one of the reasons we have called such attention to the issue of senility. None of us wants to live long if we don't live productive, effective lives in which we have minds that are clear and in which we can identify and relate to our families.

ALZHEIMER'S DISEASE

Senator RUDMAN. I want to move on to follow up a comment of just a moment ago. There was a recent report in the public press that the effects of Alzheimer's disease cost in excess of maybe $30 million a year to institutionalize and to care for that and other forms of senility.

Do you believe that is an accurate statement or do you believe that we will be doing some things that will essentially retard the expansion of that disease?

Dr. BUTLER. The actual figures are not easy to determine. Let's put it this way: Last year, this Nation had nursing home costs of $22 billion. We believe that one-half of the 1 million people in nursing homes suffer from senile dementia. They may have other diseases, but the one that makes it so difficult for them to remain in their own homes and take care of themselves is the one that so adversely affects their intellectual abilities. With this condition, they may take wrong medications, leave the stove on, or wander confused in the street. So one-half of $22 billion or approximately $10 billion a year, is estimated to be the cost of Alzheimer's disease in this country.

In addition to the 500,000 people in nursing homes who have that disorder, we believe there are another 1 million who live in the community, and who are taken care of by their family, but at considerable cost. So it is conceivable that the range you mentioned is accurate.

More to the point, I think, is that by 1990, 8 years from now, the Health Care Financing Administration projects nursing home costs alone in excess of $75 billion.

IMPACT OF CONTINUING RESOLUTION

Senator RUDMAN. Finally, I would like your frank assessment of the impact of the 1982 Continuing Resolution which imposed, as you know, the lower of the House or Senate figures and reduction of 4 percent beyond that.

Dr. BUTLER. The administration policy is directed, as you know, to the effort to provide continuing support for biomedical research, to move the country forward continuously in terms of acquiring new knowledge. The continuing resolution figure is less than the President's budget for fiscal year 1983.

This has required, naturally, strong efforts on our parts to be austere and to hold down certain types of costs. For example, we have had to delay a variety of program development activities related to the extension of research on senile dementia. We have also slowed down the admission of women to our Baltimore longitudinal study. You will recall that I mentioned there are many more women than men in the older age group included in nursing homes. These are areas in which we have curtailed our efforts, but we all share in this effort to deal with the reality of austerity.

Senator RUDMAN. I wonder if there is any outlook for savings in operations and program management in light of these. Even though we are having some growth here, there still are constraints. Great sums of money are certainly needed for research. That is the priming area where you obviously want to direct your funds. Yet, you do have operational costs, management costs.

Has any thought been given to ways of reducing that administrative overhead?

Dr. BUTLER. Yes; I know NIH as a whole has thought about it very seriously, just as we have in our own small Institute.

As a small Institute, we have perhaps had somewhat less negotiating room. Our efforts have related to reduction of program development activities, delay of various scientific opportunities, and in trying to find ways to cut costs in management areas.

We have our own separate laboratories in Baltimore, and our own staff is working very cooperatively in such simple, but not unimportant matters as turning off the lights. We are continually making efforts in a variety of areas—such as publication and travel costs—to reduce our expenditures.

TEACHING NURSING HOMES

Senator RUDMAN. Finally, what is the status of your plans to fund a teaching nursing home? And how much money has been spent to date, and how much is intended in this year's appropriation?

Dr. BUTLER. On the positive side, we have had an incredible response from the American research community, and have received 23 letters of intent. However, as a result of the continuing resolution, it was not possible for us to support any teaching nursing homes during fiscal year 1982. Wishing to be responsible to those many institutions which expressed an interest, we recently published in the NIH Guide to Grants and Contracts a notice that the funding of teaching nursing homes would be delayed until fiscal year 1983. At that time, within the President's budget, we would be able to support only one teaching nursing home.

PREPARED STATEMENT AND SUBMITTED QUESTIONS

Senator **Rudman**. We have a number of questions that we will ask you to answer for the record which will be open at such time as the transcript of your testimony is finished.

Of course, the committee wants to thank you very much, Dr. Butler, for all of your efforts and wish you every good luck in your new challenging assignment.

Dr. **Butler**. Thank you. I appreciate that.

[The statement and the following questions which were not asked at the hearing but were submitted for response for the record follow:]

STATEMENT OF ROBERT N. BUTLER

It is an honor to appear before you, to report on recent progress in aging research and to present the budget request for 1983.

The National Institute on Aging is in its second five years of existence. Our first years were very productive, serving to: help change attitudes and stereotypes about the elderly; improve understanding of the basic aging process; develop expertise among faculty and improve curricula in medical schools through the Geriatric Medicine Academic Award program; assess knowledge regarding safety and effectiveness of new procedures, technology or information that affects the elderly; develop a program of behavioral sciences research which emphasizes the study of aging as part of the life continuum rather than an event that happens when a person reaches age 65; evaluate differences in the aging process in men and women with the aim of understanding why women have a longer life expectancy; develop a new intramural laboratory, the Laboratory of Neurosciences, to study basic cerebral metabolism for better understanding changes that occur normally with the aging process; and to greatly expand the research base on Alzheimer's disease and related dementias of aging.

It seems appropriate that the 1981 White House Conference on Aging was held at a time when the Institute was in its second five years and capitalizing on research advances from its first years. As you will remember, the 1971 White House Conference on Aging recommended that a national focus for aging research be developed as a free standing institute within the National Institutes of Health. Thus the National Institute on Aging came into being. The 1981 White House Conference on Aging Technical Committee on Research noted in its recommendations that research on aging is still a relatively new area and is a progressive area that requires nurturing and strengthening of financial support. The Technical Committee on Research stated that the overreaching goal of the Aging research agenda for the coming decades should be to create and make available an adequate and appropriate knowledge base about the processes of aging, the state of being old, and the utility of solutions to problems that interfere with the well being of those in the later decades of life. It laid greatest stress upon both the development of geriatrics and the conquest of forms of senility.

Knowledge gained during our first years indicate the importance of aging research to other research areas. Aging should be viewed as a lifelong process in which we all participate, so that it is seen as an ongoing event, occupying the entire lifespan and not occurring merely as the final stage of life. It is in this sense that we study the aged to learn not only about the final phase of life, but also to learn about all aspects of development. The lifespan approach has the potential for benefiting other sciences and for providing new information of value to other age groups. An example is the discovery that identical histopathological changes occur in brain tissue of those with Down syndrome and Alzheimer's disease. Patients with Down syndrome who survive into their thirties develop what must be called Alzheimer's disease, with clinical dementia and brain tissue changes. The possibility of a common genetic defect or genetic predisposition to Alzheimer's disease throws new light on both of these diseases affecting different age groups. Disorders that are more prevalent in the elderly could clearly have payoff for the understanding and treatment of disorders of the young and old alike. Also, as more is learned about risk factors for age-related diseases, such knowledge can be applied to the development of preventive interventions in young age groups.

The support of research on disease prevention and health promotion has for some time been an integral component of the NIA research efforts. Primary prevention research focuses on efforts to investigate appropriate measures to slow or possibly reverse the rate of physiological decline, to prevent or delay onset of age-related disease processes and to evaluate those psychological factors that interact with biological processes to influence health and effective functioning in middle and later years of life. For example, a number of studies have indicated that elderly people are often malnourished. An NIA supported study is designed to determine the consequences of inadequate nutrition in healthy people age 65 and over in terms of subsequent illness and longevity. The first phase of the 5 year study is revealing that many individuals are deficient in vitamin D, a vitamin required for the absorption of calcium by the body and thus important for maintaining healthy bones and preventing osteomalacia or softening of bone. This osteomalacia can complicate osteoporosis, a bone-thinning disorder common in elderly people.

Recent behavioral studies indicate that mental decline with age is not inevitable. A California longitudinal study which tested volunteers for intelligence over a 21-year period has found that most of those tested maintained, or even improved, intellectual competence as they grew older. Several factors shed light on individual variation in retention of cognitive abilities. Physical conditions, such as cardiovascular disease, can undermine cognitive function, while advantaged socioeconomic environments and flexible lifestyles and attitudes tend to maintain cognitive function. When intellectual decline does occur with age, research has shown that it can often be slowed or reversed by relatively simple training interventions. Other research supports findings that health can be promoted through changes in smoking, diet and exercise throughout the lifespan; that job complexity and challenge influence psychological functioning and intellectual flexibility throughout life; that illness can be alleviated by social supports and improved coping abilities; and that many serious disabilities can be reduced by regimens which reward activity and independence.

As I have previously reported to this Committee, the National Institute on Aging is actively engaged in the development of research programs in geriatric medicine to increase the body of knowledge in this area. Currently this program addresses research to describe such areas as anticipated risk factors, etiology and appropriate therapy for senile dementia of the Alzheimer's type, depression, osteoporosis, and benign prostatic hyperplasia. Significant progress has been made in the past decade in understanding possible causes of senile dementia of the Alzheimer's type (SDAT). The most consistent findings in studies of SDAT have pointed to a decrease in the activity of certain chemicals in the brain which comprise what is known as the cholinergic system. It is known that the cholinergic system is involved in both memory and learning. If, as indicated by the most recent work, there is a malfunction in the complex chemical interaction which converts choline in the brain to the neurotransmitter acetylcholine, then attempts to stimulate or revitalize the cholinergic system may alleviate the debilitating symptoms of SDAT. Research efforts continue to explore this hypothesis.

An important aspect of developing geriatric research is the Teaching Nursing Home. In November, the Institute formally announced the initiation of the Teaching Nursing Home Award Program which will support research conducted by academic medical centers and nursing homes on geriatric health problems in nursing homes and other clinical settings. A major goal of the program is to encourage research on health problems which are particularly prominent in nursing homes and among geriatric outpatients, rather than in acute care hospitals. In fiscal year 1983 we expect to support one Teaching Nursing Home Award.

Approximately 3 to 4 million elderly Americans suffer from some type of dementia, a group of disorders which are characterized by a decline in intellectual functioning and a significant loss of adaptive skills. Some 500,000 of these have senile dementia of the Alzheimer's type (SDAT) with global intellectual deterioration and inability to carry out the normal tasks of daily living. Approximately 50 percent of nursing home patients have dementia, a sizable fraction of whom were institutionalized for this reason. The loss of productive members of society, disruption of families, and loss of human dignity are among the incalculable costs of SDAT. Furthermore, demographic studies indicate a rapidly escalating problem. SDAT is a disease of unknown etiology. However, it is the consensus of the scientific community that dementias of aging are not an inevitable consequence of growing old; they represent pathologic disease states subject to investigation, elucidation, and treatment.

The NIA has itself taken a major step forward in research on SDAT by strengthening its intramural Laboratory of Neurosciences. In FY 1982 the laboratory initiated a small clinical research program at the Warren G. Magnuson Clinical Center, and in combination with the ongoing basic research program, is examining cerebral metabolism changes as they relate to aging and dementia. The research goal is to establish procedures for the clear diagnosis of the dementias, examine various pharmacological therapies for the retardation or possible cure of the dementias, and to search for contributing factors or causes. The natural course of aging as it affects the brain and peripheral nervous system is also being examined. These studies on brain metabolism in aging and dementia are being integrated with a formal program on pharmacology and pharmacokinetics of aging in man. This laboratory has developed a new method for measuring cerebrovascular permeability to various drugs. By establishing relationships between certain characteristics of drugs and the degree and speed of permeation they exhibit, it will be possible to predict entry into the brain of drugs with differing physical properties. Another development is a reversible osmotic method to allow normally excluded drugs to penetrate the blood-brain barrier. Both of these developments may be useful in treating the dementias of aging.

Research conducted by other NIA scientists at the Gerontology Research Center indicates that common notions about the inevitability of activity-limiting cardiovascular problems in old age are probably unfounded. Data show that the heart of an older person pumps about as well as that of a young adult. Problems related to the older heart's inability to move blood should be considered the effect of disease - such as coronary artery disease - not aging. Various ramifications of obesity in older people are also being studied. A level of overweight somewhat in excess of the commonly used desirable weight tables of 1959 appears to correlate with minimum mortality. Obesity is also associated with increased likelihood of developing diabetes mellitus.

As I reported to you last year, cost containment is an increasingly important issue that must be addressed if we are to maintain the quality of life of an ever expanding older population. The current mandate for cost containment provides the opportunity to support research in the development of the most cost-effective programs possible. The area of health care is one presenting the greatest challenges, since medical inflation is rapidly increasing, and the elderly have high utilization of most types of medical services. With a large percentage of public (medicaid) money targeted for nursing home care, for example, cost-effectiveness studies of all long-term care possibilities need to be undertaken. The National Institute on Aging devotes a major portion of its research budget to areas relating to long-term care. Currently, the Institute is involved in research on senile dementia, urinary and fecal incontinence, falls and their associated fractures, infectious diseases, and other conditions which may effect the need for institutionalization and patient health in long-term care facilities. Through its Epidemiology, Demography and Biometry Program, the Institute is also involved in a variety of research projects which may affect future need for long-term care.

A major research need is new knowledge to develop and validate indices of human performance in terms of functional rather than chronological age, thereby enhancing opportunities for productive and satisfying work and other activity in later life. A major emphasis of our behavioral sciences research program is on health and effective functioning during the middle and later years. The Institute is currently soliciting research projects designed to specify in detail how behavioral and societal processes, interacting with biomedical processes, influence particular aspects of health and functioning as people age.

Mr. Chairman, the FY 1983 budget request for the National Institute on Aging is $84,556,000.

BIOGRAPHICAL SKETCH

Dr. Robert Neil Butler is currently the Director of the National Institute on Aging, one of the eleven research institutes at the National Institutes of Health in Bethesda, Maryland. Dr. Butler left private and consultative practice in psychiatry to join NIA on May 1, 1976. During his research, academic and service career he has served as a consultant for the U.S. Special Committee on Aging and the

National Institute on Mental Health; held faculty positions at the Howard University School of Medicine, the George Washington University School of Medicine, the Washington School of Psychiatry and the Washington Psychoanalytic Institute; and has conducted research as a psychiatrist with the National Institute of Mental Health (1955-1962) and the Washington School of Psychiatry (1962-1976). He is the author of four books and has won the Pulitzer Prize for Why Survive? Being Old in America, (1976).

Dr. Butler received his B.A. from Columbia University in 1949 and his M.D. from Columbia in 1953, served his residency at the University of California and became a diplomate of the American Board of Psychiatry and Neurology in 1961. He is the author of several articles, a veteran of the U.S. Maritime Service, and a member of many professional organizations.

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

LIFE SPAN

Question: We understand that some scientists are now saying that we are on the verge of extending the average human life span to 85 years but that may be as far as we can go. What is your reaction to this?

Answer: As a way of answering your question, let me first clarify what is meant by life span and life expectancy. Life span refers to the maximal inherent or natural life span of a particular species. In the case of man, it is thought to be in the range of 100 to 110 years of age. Life expectancy is a projection from birth to length of life using any given year as a base point. Research supported by NIH as a whole has contributed the extension in average age from 47 in 1900 to approximately 85 today. In an article in The New England Journal of Medicine, Drs. Lawrence Crapo and James Fries are pessimistic that life expectancy can be extended beyond what they consider the biological limit of 85 years. We feel that a specific limit of 85 years is not supported by biological evidence. In the last 10 years, we have made considerable progress in lengthening the average life expectancy, and it is our opinion that this will continue as a result of progress in medical research and the better delivery of health care.

Question: What drugs or other scientific developments are you working on that will help to extend life or provide "super-longevity?"

Answer: We are developing the technology to assess interventions in aging processes that may lead to both qualitative and quantitative increases in longevity. Using biological markers of aging to assess the effects of various interventions was the subject of a recent NIA conference and a forthcoming book reporting the proceedings. We are currently supporting a number of grantees who are looking at specific interventions. For example, Dr. Arthur G. Schwartz at Temple University is investigating the effect of the hormone dehydroepiandrosterone on the longevity of mice. At the University of Alabama, Dr. Raymond Hiromato is examining the effect of thymic hormones on immune function in mice. In addition to studies which focus on specific interventions, many other NIA-supported research projects are relevant to interventions which may have a significant impact on improving the quality and quantity of life.

Question: The scientists who predict the extension of life to 85 also believe that these older years will be healthier? What's your analysis?

Answer: We agree that the current trend towards increasing life expectancy will also bring increasingly healthier years to our population. In other words, we are interested not only in the length of life but also the quality of life.

SENILE DEMENTIA

Question: What progress has your Institute made in the past year on the causes and treatment of the senile dementias?

Answer: The opportunity to move rapidly against senile dementia is reflected by the extraordinary promise of recent advances in brain research. These include:

- The consistent finding that senile dementia patients have a marked reduction in choline acetyltransferase (CAT) activity, particularly in those areas of the brain that are involved in memory.
- Pharmacological investigations of cholinergic agents show convincing evidence that neurotransmitters such as acetylcholine play a critical role in human memory.
- Improvements in diagnostic instrumentation--better imaging techniques for CT scanning and the development of positron emission tomography (PET) and nuclear magnetic resonance (NMR) as tools for examining local brain metabolism--provide promise for early diagnosis and detection of senile dementia.
- The recent discovery of a primate model for memory deficit similar to that of senile dementia provides an essential new tool for testing neurochemical hypotheses and various treatment regimens.
- Development of sophisticated techniques for histological (microscopic) analysis of brain tissue (including new staining methods, spectrometric techniques to analyze the aluminum and silicon content of tangle-bearing neurons, and electron probe analysis of histological material) should contribute to the discovery of senile dementia.
- One of the most recent exciting scientific leads concerning the etiology of Alzheimer's disease comes from those scientists working with slow viruses. These viruses typically require 10-20 years to produce their damaging effects on the nervous system. The recent discovery of a simple virus that does not even have nuclear material--simply referred to as prion--gives us a very important clue to what might be happening in the pathogenesis of senile dementia of the Alzheimer's type.

Question: How well are you staffed up with researchers to go after promising leads?

Answer: We are doing reasonably well. At present there is a significant cadre of well trained neuroscientists in this country who could easily take advantage of the scientific leads in this area of research if opportunities and funds were made available to them.

ALZHEIMER'S DISEASE

Question: We hear much about the devastating effects of Alzheimer's disease, sometimes called premature senility. What progress are you making in finding drugs or other means to mitigate its effects?

Answer: There is some evidence that intravenous administration of physostigmine (a drug which prevents the otherwise fast breakdown of the neurotransmitter acetylcholine) significantly improves performance on a test of visual recognition. This indicates that the acute augmentation of cholinergic activity in patients with Alzheimer's disease can partially reverse the memory deficit of that disorder. These preliminary results are very encouraging because they indicate the potential for a pharmacological approach to the treatment of this condition.

Question: What chances are there of finding a cure?

Answer: Finding a treatment for Alzheimer's disease is within the realm of reality if we can rapidly capitalize on promising research leads and the excitement in the scientific community concerning the real possibility of treating and preventing this disease.

Question: How much do you plan to spend on research in this area in fiscal 1982 and 1983?

Answer: In fiscal year 1982, we anticipate spending approximately $6,631,000 for research on senile dementia and Alzheimer's disease. In fiscal year 1983, the figure is estimated at $7,183,000.

Question: To what extent is the hope for progress against this disease dependent on a particular funding level in fiscal 1983?

Answer: The hope for progress against senile dementia of the Alzheimer's type (SDAT) depends largely upon the availability of scientific advances which can be readily exploited. Some of the research opportunities that are crucial to the battle against this disease and can benefit from a program of expedited research support are:

o Clinical and/or Pathological Studies

Recent progress in understanding SDAT has relied upon systematic correlations between clinical and pathological findings. Further studies are needed to correlate measurements of the anatomic distribution of specific Alzheimer's lesions (neuritic plaques and neuorfibrillary tangles) with physiological, cognitive and other gross behavioral changes. There is a need to determine the exact relationships among the degree of psychological impairment and such neuropathological variables as loss in cell numbers, cell types affected, changes in tissue volume, and the presence of infarcts in various parts of the brain.

Such investigators might capitalize on brain metabolism and performance data being generated by ongoing longitudinal studies in an effort to determine early signs of and establish risk profiles for this disease.

- Cerebral Circulation and Metabolism

Impaired blood flow in parts of the brain has been suggested as a causal factor in SDAT. Efforts to study the relationship between brain circulation and metabolic changes in subjects with SDAT or at risk for this disease need to be expanded. Of particular interest are studies on living subjects using new techniques such as positron emission tomography to examine local brain metabolism as well as to evaluate the effects of specific pharmacotherapeutic regimens.

- Neurochemistry

Current research on neurotransmitter deficits in SDAT needs to be expanded into pilot clinical trials aimed at replacement therapy. An understanding of the basic biochemical and neuropharmacological mechanisms and morphological changes underlying the chronic dementias is critical to elucidating the origin and course of development of SDAT.

- Neuroendocrinology

Studies directed at explaining the role of brain peptides and hormones in regulating a complex variety of biochemical functions (enzymatic, metabolic, histological, and neurotransmitter activities) are crucial to understanding some of the clinical manifestations of the dementias of old age.

- Genetics and Population Studies

Both environmental and genetic factors (such as aluminum and certain viruses) have been implicated in the origin and development of SDAT. Further epidemiologic and genetic studies are needed to clarify the possible relationships between these factors.

- Immunology and Virology

There is evidence that at least two human spongifirm encephalopathies, kuru and Creutzfeldt-Jakob disease, are caused by transferable or atypical slow or latent viral agents. It is therefore important to explore the possible role of latent or slow viruses in SDAT. There is also a need to characterize further the decline in immune function with age, since this decline might prevent the brain from protecting itself against the invasion of noxious agents, activation of a latent agent, and autoimmune brain damage.

- Drug Evaluation, Clinical Studies and Clinical Trials

Recent studies--such as the findings of a large reduction in choline acetyltransferase activity in SDAT and transient improvements in memory brought about by physostigmine--indicate that, for the first time, it may be possible to think realistically about pharmacological interventions and clinical trials for SDAT. Typically, it requires several years of careful planning to initiate a systematic drug evaluation and clinical trials program. Now is the appropriate time to start planning such studies. As an initial step, it is essential to encourage and support systematic short-term drug evaluation or clinical studies which eventually could lead to more formal clinical trials.

FRAUD AND ABUSE

Question: How effective have your mechanisms been for preventing fraud and abuse in the use of funds for research supported by your institute?

Answer: The usual process of open scientific examination has been and continues to be important as a primary means of preventing fraud and abuse in the use of funds for research on aging. This includes publication of studies that have been critically reviewed by other investigators as well as independent confirmation of findings. Reports of scientific studies are also routinely scrutinized by NIA scientific staff. More recently, an NIH-wide ALERT System has been developed to identify researchers who are under investigation for possible irregularities in the conduct of studies supported by the NIH. In addition, the NIA is currently implementing a procedure for handling inquiries or allegations of improprieties on NIA-supported projects. The system described is still under review, and since only one complaint has been filed (which was immediately followed up on by scientific staff), it is too early to generalize about the effectiveness of the new procedure.

Question: What actions are taken against individual researchers or research hospitals which do not follow your directives?

Answer: There are a variety of options that may be exercised when it has been determined that a breach of regulations or requirements has occurred. These are first dealt with administratively by NIA program and grants management staff. If this administrative review indicates that further examination is warranted, the case is turned over to the NIH Division of Management Survey Review for futher action. If the case involves human subjects, it is referred to the NIH Office of Protection from Research Risks and the Division of Management Survey Review is alerted.

There are a number of possible options for action against an investigator or institution, some of which are part of the NIH ALERT System. These actions are:

- Suspend or terminate an active award, in whole or in part, in accordance with DHHS regulations.
- For a specified period of time, debar or suspend the individual or institution--that is, declare them ineligible for future contracts or financial assistance (grants and cooperative agreements)--in accordance with DHHS regulations.
- Decline funding of future noncompeting grant awards or research and development contracts in accordance with current delegations of authority for funding decisions.

- For a specified period of time, require special prior approval by NIH of particular research activities as a condition of future awards.

- For a specified period of time, require that an institutional official other than the principal investigator or project director certify the accuracy of reports generated under an NIH award and/or provide assurance of compliance with particular policies, regulations, guidelines, or special terms and conditions.

- For a specified period of time, "flag" all new and renewal grant applications and contract proposals from affected applicants to ensure that the pertinent Bureau, Institute and Division Director(s) and the Associate Director for Extramural Research and Training, NIH, consider all relevant investigative findings prior to a funding decision.

- Share investigational findings, including associated commentaries and rebuttals from the affected individual and/or institution, with other relevant federal agencies (such as ADAMHA, FDA, and NSF).

- Require that the appropriate National Advisory Council(s) conduct a special review of current awards to affected grantees with a view toward determining whether funding should be continued.

- For a specified period of time, share investigational findings, including associated commentaries and rebuttals from affected individuals or institutions, with Initial Review Groups and National Advisory Councils when they consider requests for further funding from those individuals or institutions.

- For a specified period of time, decline to invite affected individuals to serve on NIH peer review committees or other advisory groups.

Question: What are your mechanisms for detecting fraud and abuse?

Answer: The mechanisms for detecting fraud and abuse include: peer review of grant proposals, publications, and progress reports submitted as parts of competing renewal applications; regular administrative review by NIA program and grants management staff of annual scientific progress and fiscal reports; participation in the NIH-wide ALERT System; and formalized intra-institute procedures for receiving and investigating unsolicited allegations of improprieties and misconduct by grantees and contractors.

TEACHING NURSING HOME

Question: How much has been spent on this project to date—and how much will be spent in fiscal 1983?

Answer: The teaching nursing home program is still in its preliminary stages. To date, 23 letters of intent to submit a grant application have been received. The applications will be reviewed in January 1983 and the first Teaching Nursing Home Award will be made in mid-1983. The President's Budget includes $340,000 for this award.

Question: What would be the total cost of this project?

Answer: Total cost of the teaching nursing home program will depend on the number of teaching nursing home awards made and the duration of their existence. Ultimately, we would like to support a minimum of 10 teaching nursing homes. The most recent estimated cost for a program of this size is between $5,000,000 and $7,000,000 per year. There would, of course, be some variance in future years due to inflation.

Question: What information do you hope to get from this effort --and to what end will it be put?

Answer: The purpose of the teaching nursing home program is to provide the information necessary to prevent or improve treatment of the major chronic disorders of the elderly that are responsible for nursing home admission, as well as those problems to which nursing home residents are particularly susceptible. As evidenced by the letters of intent received by the NIA, the medical research community has the desire and ability to conduct the much-needed research on problems such as senile dementia, incontinence, decubitus ulcers, and osteoporosis that impose a large (and growing) financial and human cost to the Nation. The teaching nursing home program is designed to provide the necessary support for this research, which can contribute to the containment of the mounting multibillion-dollar costs for nursing home care, as well as to the improvement of the health of the Nation's elderly.

Question: In view of the fact that nursing home costs account for 40 percent of Medicaid reimbursements, and that nursing home costs are expected to rise in a shocking $75 billion by 1990, isn't the budget proposal to fund only one teaching nursing home woefully inadequate? How many teaching nursing home awards could be effectively utilized over the course of the next two to three years?

Answer: Many academic medical centers and nursing homes have a strong interest in expanding clinical research on nursing home problems. Given the current interest, one teaching nursing home clearly will utilize only a very small fraction of the research resources which could be applied to these problems. Nonetheless, it is important and necessary to consider the fiscal constraints of the current economic climate. We are concerned that investigator initiated research project grants, which are the mainstay of the extramural program, be protected from undue decline. Nor do we want to sacrifice overall program balance. At the same time, the teaching nursing home is a concept with far reaching implications for geriatric medicine which should not be delayed. The Teaching Nursing Home Award to be funded in fiscal 1983 will, we hope, be the first of a series of such awards. Over the next two or three years, as many as 15 such awards could be effectively utilized.

SHORTAGE OF GERIATRICIANS

Question: What funds are proposed to be available to the NIA in Fiscal Year 1983 to help ameliorate the current shortage of health professionals in geriatric medicine?

Answer: In fiscal year 1983, the Institute has budgeted approximately $1,830,000 for Geriatric Medicine and Dentistry Academic Awards. This includes $300,000 to fund four new competing awards.

CARE OF THE ELDERLY

Question: In the seven years that the National Institute on Aging has been in existence, what has been learned about care of the elderly? What do you foresee for the next six years of the Institute's life?

Answer: In its first seven years, the National Institute on Aging has made many inroads in acquiring knowledge about basic processes of aging and the care of the elderly. The most important conclusion to be drawn from the results of NIA research is that disease and disability, not aging, take the greatest toll on health in later life. Specific knowledge gained about care of the elderly are:

- The notion that serious decline in old age is the inevitable fate of the healthy mammalian brain has been challenged by scientists at the NIA's Gerontology Research Center (GRC). Based on experiments in rats, the researchers believe that--in the absence of disease, trauma, or overwhelming stress--the aging brain does not become exhausted. Over time, the brain may lose neurons or may sustain some damage, but it has the capacity to compensate and keep going. Among the adjustments the aging brain can make is to create new cell connections to make up for lost cells.

- Direct evidence that tissue of the aging heart benefits significantly from moderate exercise has been obtained through GRC experiments in rats. These investigations also show that the tendency of the aging heart to stiffen, to take longer to contract, and to spend less time relaxed can be overcome by a relatively light exercise regimen.

- A survey of the effects of estrogen on the incidence of bone fractures in older women revealed that women who had used estrogen preparations for 6 years or more had a 50 to 60 percent lower risk of fracture than women who had not used estrogens. Women who had been taking estrogens for less than 6 years or who had discontinued the drugs had less benefit from the hormone treatments. However, the use of estrogen as a possible means for reducing the risk of fracture in postmenopausal women must be weighed against the increased risk of developing uterine cancer associated with estrogen therapy.

- Although the mechanisms are not yet clear, scientists believe that manipulation of the diet, at least in animals, plays a role in the regulation of the immune system. Dietary restriction markedly decreases the frequency of mammary tumors in a mouse strain that is prone to such tumors when fed an unrestricted diet. The mice fed restricted diets also had lower levels of immune complexes (a harmful combination of antibodies and antigens) in their blood. This may be a significant finding in light of other studies showing that the level of circulating immune complexes in the blood normally increases with age.

- Using the familiar eye chart to test older people's vision may significantly underestimate their eye problems. A comparison of groups of healthy young and old adults judged to have normal or near-normal vision revealed that the greatest performance differences were in the ability of the older subjects to see large objects and to detect moving targets. Such deficits might make it difficult to distinguish a figure from its background to recognize a familiar face; it may even affect an older person's balance and coordination.

- Diabetes may not be as prevalent in the elderly as was previously thought. Performance on a standard glucose tolerance test (used to diagnose diabetes) was found to change with age. A decrease in the ability of older persons to clear glucose from the bloodstream was found to be normal and benign within certain broad limits, indicating that an adjustment for age must be taken into account. If it were not, an unreasonably and unacceptably high percentage of otherwise normal individuals would be classified as diabetic.

- The final report of the Duke Longitudinal Studies (1955-1960), along with other studies, underscores the principle that aging consists not only of biological, but also of psychological and social processes. As people grow older and change biologically, they also accumulate experiences, attitudes, coping repertoires, differential levels of social support, and varying relationships with relatives and other people. The recognition in recent decades of the far-reaching importance of the brain to the endocrine, immune, and other physiological systems--themselves changing with age--has led to recent developments in neuropsychology. It has also led to research on age-related accumulation of behaviors and social stress reactions which feed through the brain and the mind to affect these other systems.

- One of the most dramatic research findings in recent years shows that the functional capacities of workers are specifically related to the challenging complexities of the workplace. Workers of all ages respond positively to complexity. Moreover, intellectual decline with aging (when it occurs) can often be slowed or reversed by relatively simple training interventions. Old people's performance on tests of intelligence has been shown to improve with added practice on the tests, with instructions about strategies for approaching the problem, and with incentives introduced to increase motivation and attention. There is also evidence that physical training not only enhances physical well-being, but also improves intelligence and conscientiousness and reduces anxiety levels. It has also been demonstrated that older people can--and often do--learn to compensate for declines in reaction time, memory, and other age-related deficits by using mnemonic strategies or by exercising care and persistence.

- Age-related changes in the central nervous system of humans and animals may be caused by breakdown of the blood-brain barrier, which restricts exchange of water-soluable drugs and proteins between the blood and brain. A new method has been developed to measure permeability of the blood-brain barrier and the rate at which certain drugs enter the brain. This is very important because older persons tend increasingly to react adversely to drugs that affect the central nervous system. It will now be possible to distinguish what causes such adverse reactions.

- Digoxin, a drug commonly prescribed for the treatment of chronic heart disease, appears to be ineffective in certain elderly patients. There is new evidence that the drug can be safely discontinued in a high percentage of patients with stable, chronic, congestive heart failure and normal heart rhythm. Since digoxin may be toxic if the normal dosage is exceeded by even a small amount, it is thought that many patients are being exposed unnecessarily to a risk that carries no benefit.

- Recent research advances are providing clues to the possible cause of senile dementia of the Alzheimer's type (SDAT). There are consistent findings that SDAT patients have a marked reduction in choline acetyltransferase (CAT), the enzyme instrumental in the production of the neurotransmitter acetylcholine. This change in neurochemical activity correlates with changes in memory and orientation, and also with the number of characteristic lesions seen in the brains of SDAT victims at autopsy. Research efforts are now directed at supplementing the brain's supply of choline.

Over the next several years, the Institute will concentrate on means of improving the health of the older population and the alleviation or amelioration of many of the disabilities currently associated with old age. Toward this end, increasing emphasis will be placed on clinical research. This will be highlighted by the teaching nursing home program, which will support research conducted by academic medical centers and nursing homes on geriatric health problems in nursing homes and other clinical settings. A major goal of this program is to encourage research on health problems which are particularly prominent among nursing home residents. We also plan to establish specific programmatic activities related to common clinical problems of older patients. Targeted areas include pharmacology, dermatology, infectious diseases, vaccinations, urinary incontience, falls, arthritis, osteoporosis, senile dementia, and benign prostatic hypertrophy.

In addition, the Institute will stimulate research that specifies the conditions under which health may be maintained and disabilities prevented, postponed, or reversed up to the end of the life span. Topics for further consideration include: how to encourage people to adopt healthy behaviors and lifestyles before they reach old age; how to compensate for age-related deficits and impairments; how to design community facilities to delay illness and impairment of functioning in the elderly and promote independent living; and how to dispel false sterotypes of older people and improve attitudes and behavior toward the aged among medical and health care personnel.

CLINICAL CENTER

Question: In view of strong congressional support, and a commitment by Dr. Fredrickson to provide a six-bed unit to the NIA at the Clinical Center, why have these beds not been activated?

Answer: There are two basic reasons why the beds have not been activated: space and positions. In April 1981, the Director, NIH, made a commitment to the NIA for a six-bed unit and laboratory space for our Laboratory of Neurosciences in the Clinical Center and the Ambulatory Care Research Facility (ACRF). We expect to occupy the laboratory space in the Clinical Center by the summer of 1982 and the additional laboratories in the ACRF during the summer of 1983. We had expected to begin preparation of the space for the six-bed patient care unit early in 1982 so that it would be available for patient occupancy when the first laboratories become available during the summer of 1982. The NIH has identified several options to accommodate our request for beds. We have considered the options carefully and have concluded that the assignment of beds scattered on more than one ward to hospitalize patients who may be severely demented is not appropriate. This clinical program will focus on the pharmacology of aging and dementia. We feel strongly that the six-bed patient care unit should be placed in a single location where it can be operated efficiently and with the necessary medical and scientific staff. Having a single unit will facilitate close supervision of the staff in a therapeutic setting which can be controlled. Such an arrangement would also allow the unit to be closed off if it contains patients who are severely demented and require close monitoring. Linked to the assignment of space is the requirement that approximately 15 support positions for the Clinical Center be provided. The Clinical Center's bed occupancy has been, and is currently limited, by the number of nursing staff, and the Clinical Center will not be able to support the operation of the NIA unit without the provision of these additional personnel. I have discussed with the Acting Director, NIH, our need for assignment of 15 additional positions in FY 1982 for the operation of this unit.

SENILE DEMENTIA INITIATIVE

Question: About two years ago, the Department of Health and Human Services identified 10 priority initiatives, one of which was to significantly expand research on senile dementia. Has this Administration maintained that initiative, and if so, what additional efforts could be made to more fully exploit current research opportunities?

Answer: Two years ago, the Department of Health and Human Services did identify 10 priority initiatives as a possible mechanism for formulating integrated budgets around a number of significant health research problems. Since then, the National Institute on Aging has developed plans to expand research support on senile dementia of the Alzheimer's type, one of the 10 priority areas, and to capitalize on promising research leads. In FY 1979, the institute obligated $4,624,000 for senility research; in FY 1981 $5,196,000 was obligated; and for FY 1983 an estimated $7,183,000 will be obligated. This level projected for FY 1983 will allow the NIA to maintain a proper program balance within the request of $84,556,000.

RESEARCH GRANTS

Question: According to the information I have, under the 1983 budget level, the Institute can fund only 15 percent of approved new and competing research grants, as compared to 27 percent this year. Why does the award rate drop so precipitously?

Answer: Because we project the ability to fund 162 competing research project grants in 1982, an increase in the number of noncompeting research project grants will occur in 1983. This, together with an increase in the average cost of these grants, will mean substantially fewer dollars available for competing awards within the budget request. Since the number of approved applications is expected to remain unchanged, the ratio of funded applications to approved applications declines.

BUDGET REDUCTIONS

Question: In the present atmosphere of budget austerity, what programs have you had to cut back or discontinue because of lack of funds?

Answer: Basic investigator-initiated research--the research project grants line--will be cut back in fiscal year 1983. Forty-seven fewer competing awards will be funded, and the total number of competing and noncompeting research project grants will drop by 22 awards. Additionally, there is a proposed 10 percent reduction in reimbursement for the indirect costs associated with research grants. Particularly hard hit is the "Other Research" category. Fiscal constraints have required a sharp reduction in the number of competing Geriatric Medicine and Dentistry Academic Awards and have precluded funding of new awards such as the NIA Academic Award. Although some competing small grants will be awarded in fiscal year 1983, full implementation of the small grants program will be delayed.

Question: What impact has this had on your research programs?

Answer: The major effect has been a slowing of the momentum aging research has gained over the last five years. While ongoing projects are protected and will continue to be funded (though at reduced levels), fewer competing projects will be supported. This affects not only the total amount of research devoted to aging and the aged, but also the type of research and the speed with which problems basic to the field of aging research can be investigated, new knowledge gained, and solutions proposed.

Question: What impact has this had on your training programs?

Answer: In fiscal year 1981, the Institute supported 163 trainees. In fiscal year 1982, the number of trainees will drop to 157 and in 1983 to 156. The problem is compounded by the fact that fewer and fewer new awards can be made. For example, from 1982 to 1983 only one less trainee will be supported. However, the net loss of one trainee represents 11 fewer competing trainees offset by 10 additional noncompeting trainees. A result could be discouragement of much-needed new investigators from entering the field of aging research.

GRANTS COMPARISONS

Question: What accounts for your budget decision to reduce competing grants by 47 (from 162 to 115) in fiscal 1983?

Answer: We continue, as do all the NIH Institutes, to place major emphasis on the research project grant line. In FY 1983, for example, over 58 percent of our total budget, $49,333,000, will be devoted to competing and noncompeting research project grants. Because we project the ability to fund 162 competing research project grants in 1982, an increase in the number of non-competing research project grants will occur in 1983. This, together with an increase in the average cost of these grants, will mean substantially fewer dollars available for competing awards, within the budget request. It is imperative to maintain other categories of research such as the Geriatric Medicine and Dentistry Academic Awards, the Research Career Development Awards, and the small grants program. The two former awards are proving valuable in the development of curricula in geriatric medicine and dentistry, which will ultimately translate into better diagnosis and treatment of medical problems of the elderly. The small grants program provides short-term support for pilot studies, testing of new techniques, and feasibility studies of innovative research. We also consider it highly important to implement the teaching nursing home program in fiscal 1983. The teaching nursing home is intended to provide the same incentive for teaching and research on chronic diseases in the nursing home environment that teaching hospitals provide for acute medical disorders. The program will thus influence not only the development of geriatric curricula at medical schools, but also the practice of geriatric medicine itself.

Question: Does this indicate you are less interested in the coming year in other activities than new research efforts?

Answer: Our overall concern has been to develop and maintain a balanced program. Major emphasis has been on the individual investigator-initiated research project grants. Other mechanisms are also important, however, particularly as they relate to translating the results of basic research into treatment and prevention capabilities. Examples of the latter include the Geriatric Medicine and Dentistry Academic Awards and the Teaching Nursing Home Awards. Other important areas of funding include the National Research Service Awards, which train future investigators, and contracts, which provide research resources for Institute awardees and allow the NIA to support types of research which may not be amenable to the grant mechanism.

Question: What accounts for the drop of 17 in the number of renewal research grants you plan to fund?

Answer: It is Institute policy to fund renewal grants with priority scores falling close to the funding cutoff point. However, renewal grant applications have historically had poorer priority scores than new grant applications have. Given the relatively small number of competing applications which can be funded in fiscal 1983, we consider it particularly important to fund only the very best grant applications. This means that we will not fund some renewal grant applications which would have been funded as ongoing research in better times.

Question: On the other hand, intramural research, direct operations, and program management are all scheduled to get increased spending levels. Any comment?

Answer: Administrative mandatories account for a major portion of these increases. The mandatories include such items as the cost of the 1982 pay raise, within-grade pay increases, and the increased cost of the Gerontology Research Center's maintenance contracts. The Gerontology Research Center, located in Baltimore, must independently provide for many of the services which the Bethesda-based NIH components receive centrally. These services include such activities as housekeeping and general maintenance, utilities, radiation control, medical support services provided by Baltimore City Hospitals, security and trash removal. Of particular consequence in fiscal year 1983 is a newly implemented charge for indirect costs by Baltimore City Hospitals for its medical support services contract. In addition to the administrative mandatories, direct operations and program management each received an increase in funds to cover administrative costs associated with the new teaching nursing home and small grants programs.

GERIATRIC MEDICINE

Question: There is some concern that the problems of the elderly patient do not receive adequate attention in most medical school curricula, and that physicians are not being prepared well enough for the special needs of these patients. What is your comment?

Answer: We agree that until very recently, medical schools in the United States did not seriously feature gerontology and geriatric medicine in the undergraduate medical curriculm. In view of the fact that the number of older persons (and their percentage of the total population) in this country has tremendously increased in the past few decades, and that life expectancy has also risen, it is imperative that the medical profession pay particular attention to the newly emerging field of geriatric medicine. Knowledge of the special considerations in treating the elderly will enable physicians to evaluate better the health status of older patients and to treat them more effectively when they become ill. The medical school is perhaps the ideal setting for introducing gerontology and geriatric medicine to the future physician. The first 2 years of basic science training are the time to acquaint students with modern theories of aging and fundamental concepts of gerontology. The third and fourth years should include clinical experience with diseases which are commonly associated with aging and other problems of the elderly, as well as exposure to older people who recover from illnesses and cope with disabilities. This arrangement of the medical school curriculum has been of prime concern to the NIA, which has made substantial contributions to the development of geriatric medicine as a credible and accepted academic discipline in the United States.

Question: Are there enough physicians being trained to care for the growing number of elderly people in our society?

Answer: Recognizing that medical education in the care of the elderly is deficient, the NIA established the Geriatric Medicine Academic Award in 1978. This program provides financial support to medical schools for the development of curricula in geriatric medicine at the undergraduate level and for the educational development of the principal investigator into an expert geriatrician. To date we have made 23 such awards to medical schools throughout the country and are gratified at the progress made in each institution. An evaluation of the program was begun earlier this year to determine the extent to which the Geriatric Medicine Academic Awards have advanced the field of geriatric medicine among medical students and house officers as well as the career development of principal investigators and other medical faculty.

In addition to the NIA's efforts, the Veterans Administration, National Institute of Mental Health, Administration on Aging, private foundations and other private and public groups are making serious attempts to expand the training in geriatrics given to medical and postgraduate students. Despite increases in such programs since 1978, education in geriatrics is still less than optimal; according to a study led by Alan S. Robbins at UCLA, fewer than half of the Nation's medical schools have discrete courses in geriatrics for medical students. Robbins and his colleagues point out that the quality and quantity of training in geriatric medicine still requires improvement, but currently available fellowships and postgraduate educational opportunities will not meet projected manpower needs of this country.

Question: To what extent is there a shortage of researchers interested in gerontology research?

Answer: Although there is evidence of growing interest in the production of geriatric manpower at academic medical centers, much remains undone. As a result, there is a shortage of research personnel to conduct clinical and other critical research upon which the improvement of geriatric services to the elderly ultimately depends. It has been estimated that the U.S. requires approximately 900-1000 additional academic geriatricians who would constitute a cadre of investigators with the requisite research training to conduct studies on a variety of diseases and conditions which are frequently associated with the aging process, including senile dementia, diabetes mellitus, nutritional problems, urinary incontinence, emotional disorders, osteoporosis, neuroendocrine factors, emphysema, hypertension, pneumonia, and the effects of adverse reactions to and interactions among the many drugs older people take.

Question: What is being done by your Institute to increase awareness of the country's physicians about the problems of the elderly?

Answer: Since its inception, the NIA has spurred medical educators to incorporate geriatrics into their curricula and practical training programs. As a result of these efforts, professional medical societies, medical students and faculty, private organizations, and a number of other government agencies have recognized the need to promote geriatric medicine and clinical research on aging.

Among the NIA's specific activities to increase awareness of the country's physicians about the problems of the elderly are the following:

- In March 1977, the NIA held a meeting of medical school representatives to discuss the need for geriatrics to be incorporated into medical school curricula, and ways in which the NIA and other federal organizations in the field of aging could assist medical schools in developing programs in this area.

- The Institute commissioned a study by the Institute of Medicine of the National Academy of Sciences to examine the means of incorporating teaching of geriatric medicine and the extent to which geriatrics is already offered in medical school curricula. A report of this study, entitled Aging and Medical Education, was published in September 1978. A summary of the report by Dr. Peter Dans and Marie Kerr appeared in the February 1, 1979 issue of The New England Journal of Medicine and generated a great deal of interest in the complete report, which the NIA provided upon request.

- The NIA actively encouraged such organizations as the Association of Professors of Medicine, the Association of American Medical Colleges, and the American College of Physicians to recognize the need for training in geriatrics. All three organizations responded enthusiastically, and the American College of Physicians made aging the theme of its "State of the Art" series during the 1980 Annual Session.

- In December 1979, an article on "Geriatrics and Internal Medicine" by NIA Director Dr. Robert N. Butler appeared in the Annals of Internal Medicine. The Institute also submitted articles on the special medical needs and problems of the elderly to the following medical journals: Geriatrics, Journal of the American Medical Association, Resident and Staff Physician, American Health Care Association Journal, Journal of Gerontological Nursing, Hospital Practice, The Internist, Physician and Staff Journal, Forum on Medicine, Medical Times, and the medical journals of New York State, Connecticut, Tennessee, and Philadelphia. The publication of articles in these journals, which reach a large number of physicians in this country, has greatly increased physician awareness of geriatric medicine.

- In 1978, the NIA established a Geriatric Medicine Academic Award designed to stimulate faculty and curriculum in geriatric medicine and research. In Fiscal Year 1983, it is estimated that 27 awardees will receive $1,830,000.

- Finally, the NIA has published several brochures on geriatric medicine which its Information Office has distributed to physicians, medical students, and other interested individuals. Observations on Geriatric Medicine is a firsthand assessment by a practicing geriatrician of the health care needs of the elderly in the United States. Perspectives on Geriatric

Medicine includes interviews with leaders in the field of geriatrics to focus attention on the increasing need for training in the health care of older Americans. Progress Report on Geriatric Medicine was prepared for the White House Conference on Aging to summarize developments in this area since the NIA's creation.

RESEARCH CENTERS

Question: How much are you spending on research centers in fiscal 1982--and how much will you spend in fiscal 1983?

Answer: In fiscal 1982, we expect to spend around $161,000 on research centers. In fiscal 1983 we anticipate a funding level of $520,000 with the addition of one Teaching Nursing Home Award.

Question: What economies can be achieved in this area without impairing essential research and treatment activities?

Answer: Most of our centers funds in FY 1983 will be dedicated to support of the Institute's first Teaching Nursing Home Award. This award is considered highly important as the first step in developing a program to provide research opportunities on chronic illnesses in a nursing home environment. As such, any cutback in direct program funds could well prove detrimental to the program at its very inception. Some cost savings, however, have already been effected by a 10 percent reduction on negotiated indirect costs for center grants in fiscal 1983. This will result in a cost saving of approximately $15,000.

NUTRITION AND THE ELDERLY

Question: To what extent is your Institute supporting research on how dentition problems relate to the nutrition of the elderly patient?

Answer: At present, the NIA supports a modest amount of research in this area. One of the most pressing needs is for good baseline data on the extent of the problem. This issue is being addressed as part of a wider health-related study supported by the NIA. Contracts have been awarded to three different groups, each of which will identify and characterize a population of elderly individuals. Several types of information are being sought from these individuals including information on their dental status. The intent is for this study to provide sufficient baseline information to identify conditions with and indicate their prevalence so that other researchers can plan studies in greater depth in areas of their expertise. For example, once those individuals who are denture wearers have been identified, a more detailed study can address the question of the effects of dental status, including denture use, on nutrition.

In addition, the NIA is the lead agency in an interagency agreement with the National Center for Health Statistics for a followup of those HANES I study participants who were between the ages of 25 and 74 at the time of the original study. The followup is designed to relate the data previously collected on individual health and nutrition characteristics and practices to subsequent health and nutritional status, illness, and death. Questions on dental status, denture use, and diet are included. The followup study will include approximately 15,000 individuals who are now between the ages of 35 and 85, approximately 2,000 of whom are 65 years of age or older.

Question: Do you coordinate with the National Institute on Dental Research?

Answer: When appropriate, such coordination does occur. The major cooperative activity at present involves the Geriatric Dentistry Academic Award. This award was instituted by the NIA in cooperation with the NIDR; funding is by the NIA. The purpose of the award is to improve the curricula of dental schools in the area of geriatric dentistry and to encourage dental research in areas especially relevant to the elderly. To date, six awards have been made. It is anticipated that by encouraging improved training of both health care professionals and researchers in the area of geriatric dentistry, these awards will stimulate both better care of the elderly and more research into their special dental problems.

The NIA and the NIDR have also collaborated in the preparation of an Age Page on dental care. The Age Page is a fact sheet written in lay language and widely distributed free of charge to the elderly, their families, and others who care for or work with them.

Question: What are the interrelationships among denture wear, food intake and taste?

Answer: This is an area in need of further study. It is known that in young children taste buds occur on many other surfaces within the oral cavity as well as on the tongue. It is also known that the number of taste buds on sites other than the tongue decreases throughout childhood. In the adult the contribution to perceived taste of taste buds on the roof and the floor of the mouth is unknown. The NIA is currently supporting some research into taste in the elderly. Data on the effect of dentures are being obtained in at least one of these studies.

Information is becoming available that indicates that the quality of perceived tastes may be distorted in the elderly as a result of a differential loss of taste acuity for the qualities of salty and bitter, but not for sweet and sour. A serious problem is the excessive use of the salt shaker by some older persons with hypertension because of the decreased perception of saltiness. One can speculate on the effects such changes in perceived taste would have on food intake but more research is clearly needed.

Question: What effect, if any, does periodontal disease have on nutrition?

Answer: Periodontal disease begins as an inflammation of the gingiva (the soft tissue surrounding the teeth). This is characterized by swelling and redness and may lead to spontaneous bleeding or bleeding as a result of being touched. If untreated, periodontal disease proceeds to loss of both the soft and hard tissues surrounding the teeth. As a result, the teeth become loose and will eventually fall out. The pain and the difficulty in chewing which accompany the various stages of the disease process will surely have an effect on food intake, and thus will most likely have an impact on nutrition. It is reasonable to assume that one effect will be a shift from hard to soft foods. The NIDR has a major research program directed toward the prevention and treatment of periodontal disease. Since the disease has its onset in the early and middle adult years, and since prevention and early treatment are the best ways of dealing with this problem, the major efforts in this area will probably be directed at younger age groups. The growing problem of edentulousness (lack of teeth) in the elderly is testament to this need.

COORDINATION OF NUTRITION RESEARCH

Question: There are two institutions in the federal government designated to do research on nutrient requirements for the elderly: The National Institute on Aging and the U.S. Department of Agriculture's Research Center at Tufts University. What efforts are are you making to coordinate your research projects with others inside and outside NIH?

Answer: There are two major efforts at coordination of nutrition research in which the NIA participates. One is the NIH Nutrition Coordinating Committee. The membership includes representatives from each of the Institutes at NIH and from several other federal agencies with an interest in nutrition research. The exchange of information which occurs through this committee facilitates coordination of research efforts.

In addition, in 1980 the NIA organized an ad hoc interagency committee on research on aging for the purpose of facilitating communication and cooperation among those federal organizations involved in aging research. As its first major task, the committee is involved in aiding the NIA in an inventory of federally supported research in the area of aging.

These organized efforts at coordination provide a forum for communication among representatives of various federal agencies. Ultimately it is this communication which is the basis of effective coordination.

Question: What type of cooperation is currently going on between NIA and the Tufts Nutrition Research Center for the Elderly?

Answer: Under the terms of a 1979 Memorandum of Understanding and Agreement among Tufts University, the NIA, and the United States Department of Agriculture, the Director, NIA and/or his designate has participated actively as a member of the Executive Committee overseeing the programmatic development and research content of the USDA-Tufts Nutrition Research Center. This Committee has met approximately seven times during the period December 1979 through January 1982. Exchanges between the NIA and the USDA-Tufts Nutrition Center have consistently been open and productive, and have resulted in a mutual awarenss of program intentions, methodologies, and opportunities for collaborative endeavor.

Although the USDA-Tufts Nutrition Center is functionally quite new--most of the energy and effort having until recently been directed toward the construction of the Center's physical facilities--there are already the beginnings of collaborative programs between the NIA and the Center. Scientists at the

Gerontology Research Center (NIA's intramural program in Baltimore) and counterparts at the USDA-Tufts Center are already engaged in a retrospective analysis of dietary histories assembled on a group of relatively healthy and independently dwelling volunteers who participate in the Baltimore Longitudinal Study of Aging, conducted at the Gerontology Research Center. The joint analysis focuses on seasonal and other variations in dietary intake as a function of age.

In addition, senior members of the NIA scientific staff have aided in the development of a collaboration between the USDA-Tufts Nutrition Center and the East Boston Medical Center study of aging (which is supported through contract by the NIA). This collaboration focuses on the nutritional status of the frail elderly in the East Boston community.

As the USDA-Tufts Center occupies its new facilities and develops a wider spectrum of research activities, it is anticipated that the opportunities for collaborative effort between the NIA and the Center will grow rapidly.

NATIONAL INSTITUTES OF HEALTH

DIVISION OF RESEARCH RESOURCES

STATEMENT OF DR. JAMES F. O'DONNELL, ACTING DIRECTOR

ACCOMPANIED BY:
- **RICHARD L. SHAFER, EXECUTIVE OFFICER**
- **THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH**
- **ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

SUBCOMMITTEE PROCEDURE

Senator RUDMAN. I will now call on the Division of Research Resources.

INTRODUCTION OF ASSOCIATES

Dr. MALONE. Mr. Chairman, I have been joined by Dr. James O'Donnell, the Acting Director of the Division of Research Resources, and Richard Shafer, the Executive Officer. He is accompanied in the second row by William K. Russ, the Budget Officer, and Norman Mansfield, Director of the Division of Financial Management. And we also have with us Richard Miller, Assistant Director for Budget, Division of Financial Management.

Senator RUDMAN. Dr. O'Donnell, we welcome you to the hearing. We have your statement and would like an overview if we could have that. The entire statement will be included in the record.

Dr. O'DONNELL. Thank you, Senator. It gives me great pleasure to be here again this year to present the 1983 budget request for the Division of Research Resources.

The Division develops and supports vital multicategorical research resources which strengthen and enhance the research environments of institutions engaged in health-related research across the country. Our portfolio includes general clinical research centers, primate research centers, biotechnology resources, laboratory animal science resources, the minority biomedical research support grants, shared instrument grants, and the flexible funding available through the biomedical research support grant program.

The budget for the Division of Research Resources accounts for approximately 5 percent of the total NIH budget, but it supports about one-third of all of NIH resources and centers.

In 1981, 30 percent of all NIH grants and 25 percent, about 700 million dollars' worth, of the total NIH extramural funds, were held by investigators who were users of the DRR resources.

In total, we estimate that more than 16,000 individuals were reported using DRR resources, facilities, or services annually.

Among our activities, in addition to our resource support, we provided for research in: Nutrition in the range of $14 million; disease prevention, $10 million; diabetes research, $15.6 million.

Other highlights from the Division include the two Nobel Prizes that were awarded for investigators who did their initial work at the New England Primate Research Center, Dr. Torsten Wiesel and Dr. David Hubel, whose research was supported by the National Eye Institute.

This year, we celebrate the 10th anniversary of our minority biomedical support program, and are proud to announce that 14 minority institutions have now moved into the mainstream of biomedical research. They are receiving our biomedical research support grants. And in recognition of the program's accomplishments, we are changing its name to the minority biomedical research support program.

In these 10 years, over 4,000 students who have received MBS support are now pursuing careers in research or in the health professions.

Our animal resources program is the major NIH component which provides assistance to institutions in complying with animal welfare requirements. About $15 million in the last 10 years has been provided to institutions to help them upgrade their animal facilities.

We are also involved in assisting institutions in providing for upgrading of obsolete research instrumentation. Along with the National Institute of General Medical Science, DRR is providing support for this activity in 1982.

Our request for the Division of Research Resources is $191,024,000. It provides for expansion of our shared instrument grant program and maintenance of nearly all of our existing resources.

I would be pleased to answer any questions.

EFFECT OF THE CONTINUING RESOLUTION

Senator RUDMAN. I will ask you the same question I asked Dr. Butler toward the end of his testimony. I would like to know in your words the effect of the continuing resolution on your programs.

Dr. O'DONNELL. Under the continuing resolution, we are negotiating all our grants downward by an average of 4 percent from their commitment level. We feel that with certain economies, that our grantees can live with this reduction for 1 year, so that we can continue to support all of those awards that we had intended to fund. Our grantees can sustain this reduced level for 1 year only.

ADMINISTRATIVE OVERHEAD REDUCTIONS

Senator RUDMAN. Do you have any further capabilities within your own budget—and I have it here in front of me, and it is not a terribly large budget—to make any further administrative overhead reductions in such things as travel, consultant services, and so forth?

Dr. O'DONNELL. We are, as Dr. Butler indicates, as are all the components of NIH, looking at all of our activities relating to program management and direct operations, and are reducing wherever we can.

We estimate that we will be reducing the amount spent in 1982 by about $100,000 from what we originally estimated.

EFFECT OF INDIRECT COST REDUCTION

Senator RUDMAN. What is the impact on your research and training capabilities of the plans to put a cap on indirect costs of research if, say, 90 percent is in fact adopted?

Dr. O'DONNELL. Although we agree with the administration's position that the cost of research must be contained wherever possible, and we are concerned with the increases in the past years in indirect costs, there will be an impact, we feel, on institutions. And since this Division deals most closely with institutional kinds of programs, we have already received concern from many of the institutions that they will have to make cuts within their operating budgets.

These are real costs for institutions. And they will have to try to achieve the same kinds of reductions that we are in our operations.

Senator RUDMAN. How about the plans to hold training allowances to slightly below fiscal 1982 active levels?

Dr. O'DONNELL. We do not anticipate a significant problem in that area.

ACCOMPLISHMENT OF GENERAL CLINICAL RESEARCH CENTERS PROGRAM

Senator RUDMAN. We note that the general clinical research centers have reached their 20th year. Can you tell us briefly the accomplishments of the program since its inception, just a brief summary? It is a substantial sum of money in the budget.

Dr. O'DONNELL. The general clinical research centers program supports approximately 75 percent of the NIH extramural funded beds for clinical research. Within the past 20 years, there have been significant research accomplishments. This year, we are surveying these accomplishments and have selected 6,500 of the most significant publications in four scientific areas. We anticipate being able to deliver a report to the Congress very shortly in the first of these fields, neurosciences, followed by one in diabetes.

RECOUPING RESOURCE INVESTMENTS

Senator RUDMAN. Next, let's talk briefly about how you recoup some of your investments. We note that you have now had some efforts underway to sell or license certain equipment that has been manufactured and discovered because of research carried out by your organization. To what extent are you able to recoup any of that initial investment? What is the progress of that program at this time?

Dr. O'DONNELL. Within our biotechnology resources activity, there are several instances where instrumentation has been developed and has now been picked up by the commercial sector for development and distribution to a wider community. Examples are in several of the areas of transducers, and implantable devices, which are now being picked up commercially.

One of our computer operations, CLINFO, which is used in clinical research centers, is now commercially available and has been picked up in the commercial sector in several instances.

So within a few of our programs, there are opportunities for handoffs and further commercialization.

PROPHET COMPUTER NETWORK

Senator RUDMAN. What about the PROPHET operation?

Dr. O'DONNELL. PROPHET is another example of one of our computer operations. Several pharmaceutical houses have purchased the PROPHET software and are now utilizing this in their operations. This is totally cost-reimbursable to us when they participate in an activity like PROPHET.

Senator RUDMAN. To what extent are we recouping our costs at that level?

Dr. O'DONNELL. In any venture where we have an activity with the commercial sector, we recoup 100 percent in fees. The Federal Government is not subsidizing these commercial ventures at all.

PRIMATE BREEDING

Senator RUDMAN. I want to mention at this point the chairman of our subcommittee, Senator Schmitt, as you know, would want to be here, but was unable to be here today. He is very interested with his background, of course, in some of your primate research, and particularly interested in that which is conducted at New Mexico State University.

I am going to ask you to answer several questions that he has submitted for the record.

I would like to ask you about testimony that was given before this committee several years ago in which there was a shortage of certain laboratory animals, and you were going to start your own programs, particularly with Rhesus monkeys. And I wondered what the status of your program was in that effort.

Dr. O'DONNELL. The program in breeding the Rhesus monkey was initiated chiefly because of the import ban from India, preventing the import of any Rhesus into the United States. Under contract, we established several breeding activities and are happy to say that this year, we are to the point that we will be able to terminate one of these contracts, phasing out the Federal support. The commercial sector is able to continue providing adequate numbers of primates, particularly Rhesus, for investigators. We will no longer need to put that considerable amount of money into that activity.

We will be able to decrease about $500,000 from that activity this year.

The situation at New Mexico State that you referred to deals with a colony of chimpanzees. There is really only one activity that the Division is involved with in breeding chimpanzees, and that is at the Yerkees Primate Research Center. The Division of Research Services also has one activity that they are supporting now for breeding chimpanzees.

However, we understand that the New Mexico State University is exploring various avenues of potential support from the Federal Government.

TRAINING IN VETERINARY MEDICINE

Senator **Rudman**. A final question. I believe that in part of your submission, there is some indication you continue to provide some funds for the training, at least at the postgraduate level, of veterinarians. Is that an accurate statement?

Dr. **O'Donnell**. Yes; our formal training activity in the Division under the National Research Service Award Act is in the field of veterinary medicine to provide postdoctoral training to veterinarians so that they will be in the position to participate in research activities and give direction to animal-related research which NIH supports.

Senator **Rudman**. So the thrust of that training is quite different than the thrust of the training that we might find in an educational institution that would be training veterinarians for practice; is that correct?

Dr. **O'Donnell**. That's right. This is beyond their veterinary training. This is postdoctoral training.

Senator **Rudman**. In the research area to handle the special medical problems that arise with animals——

Dr. **O'Donnell**. Yes, sir.

Senator **Rudman** [continuing]. That are used in that program?

Dr. **O'Donnell**. Yes, sir.

PREPARED STATEMENT AND SUBMITTED QUESTIONS

Senator **Rudman**. We will have some additional questions for the record, and we would like you to provide the answers at the time that you send back your corrected transcript.

We thank you very much, Dr. O'Donnell, and your associates, for taking the time.

[The statement and the following questions which were not asked at the hearing but were submitted for response for the record follow:]

STATEMENT OF JAMES F. O'DONNELL

It gives me great pleasure to appear before you once again to present the 1983 budget request for the Division of Research Resources (DRR). This Division was established by the Surgeon General of the Public Health Service in 1962 as the Division of Research Facilities and Resources, and was renamed the Division of Research Resources in 1969. In addition to serving as NIH's primary focal point for the development, support, and administration of important research resources, used by biomedical investigators in almost all fields of biomedical science, the Division also provides technical expertise, information exchange, and efficient program management to individual investigators and to the biomedical research community in general. In other words, the Division of Research Resources provides support to strengthen and enhance the research environments of institutions engaged in health-related research through a wide variety of essential research resources. These resources include research environments and facilities, sophisticated equipment, research animals, clinical research beds, manpower development opportunities, and flexible research funds for research-intensive institutions.

The following statistics demonstrate the vital role of the Division of Research Resources within the NIH:

- The budget for the Division of Research Resources accounts for approximately 5% of the total NIH budget.
- In 1981, 30 percent of all NIH grants, and 25 percent (about $700 million) of the total NIH extramural funds were held by investigators who were users of DRR resources.
- About one-third of all of NIH support for centers and resources is funded by the Division of Research Resources.
- Institutions in which we support General Clinical Research Centers receive more than two-thirds of the NIH grants awarded to M.D.s for research involving human subjects.
- Ninety-eight hundred investigators across the country are able to initiate or extend their research activity through the use of Biomedical Research Support Grant funds. Two-thirds of these investigators have no Public Health Service support other than BRSG funds.
- In total, more than 16,000 individual investigators report using DRR-provided resources, facilities or services annually.

The Division of Research Resources provides essential support to much of the research in areas of interest which transcend the individual Institutes of the NIH. For example, in 1981 DRR, in addition to providing to resource support, also provided support for research related directly to these special interest areas in the following amounts:

- For nutrition, $14.3 million
- For disease prevention research, $10.1 million

- o For heart, lung, and blood research, $27.1 million
- o For diabetes research, $15.6 million
- o For population research, $9.2 million
- o For genetic research, $17.0 million

In recent years the Division of Research Resources has made significant advances in the conduct of biomedical research. The Minority Biomedical Research Support Program (MBS), NIH's major mechanism for providing research opportunities for minorities and minority students, is in 1982 celebrating its tenth anniversary. During this time, the number of institutions participating in this Program has grown from 38 institutions in the first granting year (1972) to a high of 81 institutions in 1981. Currently, approximately 600 faculty, 1,000 undergraduate, and 350 graduate students participate in the Program. We anticipate joint funding efforts with the Institutes of the NIH at a level of about $6 million in FY 1982 in addition to the $18 million funded by DRR. The MBS program has been successful enough in improving the research capabilities of minority institutions that eight institutions participating in the program have entered the mainstream of biomedical research with investigators successfully competing for, and receiving, research project grants.

Highlighting the 20th anniversary of the Primate Research Centers Program was the announcement of two Nobel prizes awarded to Torsten Wiesel and David Hubel, who conducted significant portions of their research at the New England Primate Research Center. Their work on how the brain interprets and utilizes signals from the outside world through the eye, is typical of the sort of preclinical studies which are most successfully done on the nonhuman primate and illustrate the importance of the proper research environment.

Over 6,500 key scientific publications have resulted from the 20 years' history of the General Clinical Research Centers Program, which describe new clinical applications and procedures for health research. The General Clinical Research Centers Review Committee has established a procedure of reviewing research protocols which assures compliance with Human Subject Regulations and provides the opportunity to observe the performance of Institutional Review Boards.

In the 20 years of its existence, DRR's Biotechnology Resources Program has evolved from mainly supporting large general-purpose computer centers in medical schools to supporting of a very broad array of technologies related to the development and application of biomedical engineering; computer science and knowledge systems; and understanding the structure and function of molecular biology. Currently, over 2,100 investigators holding $120 million worth of PHS grants are using biotechnology resources.

Particular attention is currently being called to several issues regarding research resources. In the forefront is the issue of instrument obsolescence and shortages. Evidence is growing steadily that there is a severe shortage of research equipment and instruments in laboratories conducting federally-supported biomedical research. This shortage has a negative impact on the quality, productivity, and efficiency of biomedical research. As a result, the Division of Research Resources is beginning a shared instrument grant program in 1982, which will be modestly expanded in 1983. This program will provide the recipient institutions with up to $250,000 for the purchase and installation of important research instruments which will be shared among investigators. In addition, the Biotechnology Resources Program develops and makes available high technology instruments and the newest research methodologies.

The issue of the use of laboratory animals in biomedical research is a multifaceted one. In 1981, the NIH sponsored a conference called "Trends in Bioassay Methodology," during which time the relative merits of *in vivo* versus *in vitro* experimentation were discussed. Interest within the community in developing alternatives to the use of animals has led DRR to initiate a new activity in 1983 called Biomedical Research Model Development. In 1983, this activity will consist of initiating planning efforts through workshops and conferences aimed at understanding the problems and identifying areas of research most likely to benefit from the development of models and the areas of technology most likely to yield usable research models. DRR staff have been studying this issue for quite some time, and through the experience gained in the Laboratory Animal Sciences and Primate Research and Biotechnology Resources programs, possess the technical expertise to design and administer this Biomedical Research Model Development activity.

DRR feels that there are a considerable number of opportunities for academic, industrial, and governmental collaboration in developing research resources. This Division has both past and current experiences in this area, as well as ideas for entirely new cooperative ventures, as for example, in fifth generation computer technology with particular attention to artificial intelligence. DRR staff will attempt to bring together the knowledge bases and resources of the private and public sectors for overall benefits to health research. A current example of DRR's industrial collaborations is the PROPHET Computer Network, a DRR-developed national resource which provides a wide range of sophisticated computer capabilities to over 700 academic, industrial, and government-based biomedical rsearchers at 40 sites throughout the country. The PROPHET System has involved close collaboration with industry, both to assist in defining and developing the System and its capabilities and more recently, as full participants in the use of the System. At present, the Lederle Corporation utilizes the PROPHET software on their own in-house system, and Burroughs-Wellcome, Smith Kline and French, and the Dow Chemical Corporation use the NIH-owned system in collaboration with the other academic and government-based users. In addition, the Food and Drug Administration is planning to use the PROPHET Network to shorten the time and cost required for developing new drug applications by industrial pharmaceutical organizations.

Mr. Chairman, the request for the Division of Research Resources for FY 1983 is $191,024,000. I will be pleased to answer any questions.

Biographical Sketch

Name: James F. O'Donnell, Ph.D.

Date and Place of Birth: July 22, 1928
Cleveland, Ohio

Citizenship: United States

Marital Status: Married, 1955; three children

Education:

June 1946 -	Graduated from High School
June 1949 -	B.S. (Biology), St. Louis University
Dec. 1957 -	Ph.D. (Biochemistry), University of Chicago (Thesis: An Analysis of the Acid-Soluble Fraction of Normal and T_2r-Infected Cells of *E. coli B*.)

Brief Chronology of Employment:

1953 - 1955	Graduate Teaching Assistant, Department of Biochemistry, University of Chicago
1957	Visiting Lecturer, Biochemistry, Summer, University of Colorado
1957 - 1968	Assistant-Associate Professor, Biological Chemistry and Experimental Medicine, University of Cincinnati, College of Medicine
1963 - 1964	Visiting Professor in Chemistry, Xavier University, Cincinnati, Ohio
1968 - 1969	Grants Associate, Division of Research Grants, National Institutes of Health (NIH)
1969	Health Scientist Administrator, Population and Reproduction Grants Branch, Center for Population Research, National Institute of Child Health and Human Development (NICHD), NIH
1969 - 1971	Program Director, Population and Reproduction Grants Branch, Center for Population Research, NICHD, NIH
1971 - 1976	Assistant Director, Division of Research Resources, NIH
1976 - Pres.	Deputy Director, Division of Research Resources, NIH
1979 - Pres.	Member, Senior Executive Service
1981 - Pres.	Acting Director, Division of Research Resources, NIH

Military Service

U.S. Army, November 20, 1950 - November 19, 1952

Societies:

New York Academy of Sciences
Society of Research Administrators

Other NIH Activities:

Executive Secretary, National Advisory Research Resources Council, 1971-Present
Chairman, Awards Board, Division of Research Resources, 1971-Present
Member, Extramural Forum Subcommittee, 1971-1972
Member, Editorial Subcommittee, 1971-1972
Member, Executive Committee for Extramural Affairs (ECEA), 1971-September 1979
Member, Research Subcommittee, ECEA, 1971-1972

Member, Staff Training in Extramural Programs (STEP) Committee, 1971-1974
Member, Belmont Retreat Subcommittee, 1972
Member, Subcommittee on External Training Opportunities, 1972-1973
Director, STEP Module on Committee Management, 1973
Chairman, Research Subcommittee, ECEA, 1973-1977
Member, NIH Extramural Training Advisory Committee (NETAC), 1973-September 1979
Member, Grants Associates Board:
  Liaison Member, 1970-1971
  Full Member, 1973-1977
Director, STEP Module on Grantee-Contractor Relationships, 1974
Chairman, Panel of ECEA Retreat on Peer Review, February 1974
Chairman, Panel at Grants Associates Board Retreat, July 1974
Chairman, NIH Training Design Team, 1978-Present
Member, NIH Scientific Review Group Orientation Subcommittee, February 1979-November 1980
Member, NIH Research Resources Coordinating Committee (RRCC), July 1979-December 1980
Member, Task Force on Grants Technical Assistants/Grants Clerks/Committee Management Officers, October 1979-June 1980
Member, Extramural Program Management Committee (EPMC), October 1979-Present
BID International Representative, November 1979-January 1981
Member, Review Policy Committee, January 1980-June 1980
Member, EPMC Agenda Subcommittee, February 1980-May 1980
Member, NIH Core Grants Work Group, RRCC, July 1980-November 1980
Member, EPMC Agenda Subcommittee, January 1981-Present
Member (ex officio), National Diabetes Advisory Board, January 1982-Present

NIH Training:

Federalism and Decentralization of the Executive Branch, 3 Days, December 1971
Federal Executive Institute, Organizational Development and Team Building, 5 Days, July 1972
Organizational Development/Team Building, 5 Days, January 1973
Organization Development Seminar, 2 Days, May 1973
Legislative Operations Roundtable for Executives, 5 Days, May 1973
Managing Through Face-to-Face Communication, 5 Days, December 1973 (American Management Association)
Kepner-Tregoe, Government Management Seminar, 8 Days, November 1975
Management Development Program, 3 Days, March 1976
Equal Employment Opportunity and the Federal Employee, 1 Day, May 1976
Federal Executive Institute, Executive Leadership and Management, 15 Days, September 1977
Legal Aspects of Program Administration, Legal Education Institute, 3 Days, January 1979
Federal Executive Institute, Executive Development, 2 Days, April 1979
Program for Senior Managers in Government, Harvard Business School and Kennedy School of Government, 15 Days, August 1979
Performance Appraisal Training-Phase I, NIH, 1 Day, September 1979
Data Processing for Non-DP Executives, Advanced Management Research International, Inc., 3 Days, February 1980
Basic Program Officials Guide to Contracting, DHEW, 4 Days, April 1980
Performance Appraisal and the Communication Process, NIH, 1 Day, July 1980
Anticipating the Eighties, National Institute of Public Affairs, 12 Days, March-June 1981
Briefing for Executives on Legislative Operations, Government Affairs Institute, OPM, 1/2 Day, July 1981
Advanced Seminars for Senior Executives, National Institute of Public Affairs, 6 Seminars, September 1981-June 1982

Awards:

Quality Increase for Performance from September 1973 to September 1975. Awarded October 1975.
NIH Director's Award for Performance from 1977 to 1978. Awarded June 1979.

Civic Activities:

Speakers Bureau, Ohio Board of Health, 1966-1968
Member, Board of Directors, Social Health Association of Cincinnati, Cincinnati, Ohio, 1966-1968
Program Chairman, Family Life Bureau of the Archdiocese of Cincinnati, 1967-1968
Member, Board of Directors, Community Swimming Pool, Potomac, Maryland, 1968-1970
Member, Parish School Board and Advisory Council, St. Raphael's Church, Potomac, Maryland, 1968-1971
Speaker's Bureau, National Institutes of Health, Bethesda, Maryland, 1982-Present

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QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

DRR PLANNING ACTIVITIES

Question: How has the Administration's call for budget austerity affected the DRR's planning for FY 1983?

Answer: During our planning process, the Division considered again such cost-reducing measures as increasing the use of fees for service, wherever possible; the expansion of third-party reimbursements where applicable; and the more efficient management of its activities. Consequently, we believe we are now operating important research resource programs in the most cost-effective manner.

Difficult priority-setting decisions, in which professional judgments were weighed carefully against the fiscal realities of budget austerity, have resulted in our request to expand support for shared research instrument grants. The shortage or obsolescence of research equipment and instrumentation continues to be one of the most serious impediments to biomedical research today.

Finally, we are planning an overall, corporate NIH approach towards filling the needs for multicategorical shared resources. To accomplish this, we have compiled user data indicating which NIH grantees use DRR's resources. This information, which has been widely disseminated, gives each Institute an opportunity to review their grant portfolio in terms of resource usage, and to provide DRR with advice and recommendations on their future requirements. We feel that this is working well and we are encouraged, therefore, to continue to play a more active role in overall research resource management.

HIRING FREEZE

Question: Are you still operating under a hiring freeze?

Answer: Yes, we are still operating under a hiring freeze.

Question: With what effect?

Answer: The current hiring freeze prohibits permanent or temporary appointments from outside DHHS. Requests for individual exceptions on a case by case basis for critical operations can be made, but the time and effort involved in developing the necessary documentation and the delay in gaining the final approvals creates problems for management and the individuals concerned.

We have experienced some difficulties in recent months with the recruitment of clerical support personnel. The need for clerical support personnel is a continuing and pressing one. We have exhausted the resources made available by the reductions in force in other PHS agencies. We must be in a position to recruit responsibly and effectively from outside sources, and we must be able to assure our current temporary employees that their appointments can be extended.

REDUCTIONS IN 1983

Question: What further cuts of DRR activities do you anticipate for FY 1983?

Answer: In 1983, we anticipate funding six fewer General Clinical Research Centers than in 1982; four fewer Biotechnology Resource Centers; one less Laboratory Animal Sciences Center; 93 fewer Biomedical Research Support grants; six fewer Minority Biomedical Research Support grants; one less NRSA institutional trainee; and four fewer research and development contracts. In addition to these reductions, we also plan to negotiate downward, by an average of four percent, the direct cost of all competing awards, and to reduce reimbursements for indirect costs by ten percent on all grants. This latter reduction would be implemented by NIH and other PHS agencies on an across-the-board basis by awarding ninety percent of indirect costs based on the formally negotiated rate at each institution.

In the direct operations and program management activities, we will continue to look for ways to improve management efficiencies; reduce travel and purchases of supplies and equipment in an attempt to achieve further administrative savings.

Question: How is your mission being affected?

Answer: In 1983, we will still be able to carry out our research mission, even though, at a somewhat reduced level.

REORGANIZATION OF DRR

Question: What is the current status of considerations to reorganize your agency?

Answer: The NIH, as a result of language in last year's House report, has prepared a report on the establishment of a National Biomedical Research Resources Program (NBRRP) which has been submitted to the House of Representatives. NIH is currently in the initial phase of exploring how best to organize such a program and address the issues. Currently under study are the special management problems that such a collaborative effort would present. For the envisioned NBRRP to work well, there should be broad based Institute participation in planning its priorities and establishing budgets for the program. In developing the program, the NIH will make use of special consultants such as the Advisory Committee to the Director, NIH, and the National Advisory Research Resources Council. It is anticipated that the Division of Research Resources will play a major role in the implementation of the National Biomedical Research Resources Program.

As a preliminary step in the development of the National Biomedical Research Resources Program, the Division has initiated a request to the Secretary for a name change to the "National Institute of Biomedical Research Resources". This request is currently under review and consideration within the NIH. The National Advisory Research Resources Council has strongly endorsed the name change.

Question: To what extent do you feel the Division's organization should be noncategorical in nature?

Answer: It is important to maintain a noncategorical/multicategorical resource organization at the NIH to provide the research resources vital to the conduct of all biomedical research, particularly in light of recent budgetary constraints. The programs of the Division of Research Resources serve this function by remaining multicategorical in nature. Within the biomedical research community, there exist many categorical specialities. Each categorical Institute supports specialized research related to its respective mission. As a result, the broad use of multicategorical resources which crosscut and provide vital support to all areas of research, often times are sacrificed at the expense of categorical activities within the research institutes. The Division's multicategorical nature becomes increasingly more important as research dollars become scarcer, and investigators, supported by grant funds from the categorical institutes, begin seeking access to general clinical research centers, primate research centers, biotechnology resources, and centers, laboratory animal sciences resources, minority biomedical research support grants, shared instruments, and the flexible funds of the biomedical research support grants.

BIOTECHNOLOGY RESEARCH CENTERS

Question: What accounts for your plan to reduce biotechnology research centers from 41 in 1982 to 37 in the coming fiscal year?

Answer: The costs associated with the Biotechnology Research program are increasing at a rate greater than biomedical research in general. In view of the current budget constraints, it is necessary to phase out four resources which have mature technologies in order to provide maximum support to those developing biotechnology resources that will provide maximum benefit to the biomedical research community.

Biotechnology research resource centers develop and provide access to sophisticated instrumentation and technology needed to solve biomedical and clinical research problems. Because of the rapidly changing technologies in this area of science and the problem of instrumentation obsolescence, it is vital that biotechnology research keep up with the latest state-of-the-art technologies.

Question: What will the effect of this cutback be on providing biomedical scientists with access to sophisticated instruments?

Answer: Existing instruments at centers that must be phased out will continue to be used locally. However, other major purposes of biotechnology resources, namely the development of new sophisticated instruments, collaboration of instrument technologists with biomedical investigators, training of biomedical scientists in the use of sophisticated instruments, and the dissemination of new instruments throughout the research community will decline commensurate with the phase-out of existing centers and the failure to establish new centers. We estimate that this cutback may prohibit up to ten percent of the user-investigators from gaining access to needed resources.

PROJECTS WITH INDUSTRY

Question: The subcommittee is glad to note your efforts to foster commercial development of useful equipment originally developed under your program. Please bring us up to date on this work.

Answer: The Biotechnology Resource Program requires its resources to make their capabilities available to support biomedical research in many ways. Particularly, when the market for a resource's capability is large enough for viable commercial diffusion, resource staff are encouraged to collaborate with potential purveyors to accelerate the commercial diffusion in the most effective way. This is especially important where the capability can satisfy needs of society outside the health research arena.

Recent interactions with industry have followed at least three different models. The DRR itself had developed a data management and analysis tool for clinical investigation, (CLINFO). A commercial firm is selling the system here and overseas to both research institutions and drug houses. Some of those sold are being used to analyze the progress and results of clinical trials.

Academic and industrial collaborative projects are springing up to incorporate a resource's new idea into a commercial product. This type of collaboration also gives our resources access to methods not found in academia. This collaboration is effective whether or not the capability is protected by patents or copyright.

The industrial users of the DRR PROPHET Network have developed software which they have made available to the entire user community through the Network. In particular the industrial users have made significant scientific and programming contributions in areas such as quantitative structure activity relations and pharmacokinetic analysis. The PROPHET System has also had a commercial spin-off in the RS-1 computer programs now being marketed by the Bolt Beranek and Newman Corporation.

Some recent projects developed under the BRP program that have commercial potential demonstrated or promised include:

Capability	Originator	Industry
Solid State Sensor for Blood Potassium	Case Western Reserve University	Abbott Laboratories
Data Management and Analysis for Clinical research	Division of Research Resources	Bolt Beranek and Newman
Molecular Genetics Analysis & design	Stanford	Intelligenetics
Solid State Sensor for pH measurement	Case Western Reserve University	Leeds and Northrop
Continuous positive airway pressure device for neonates	Case Western Reserve University	Sherwood Industries

Question: To what extent do you recoup your investment after getting the private sector interested in your products?

Answer: No direct recoupment to our program is sought because commercialization leads to vastly reduced costs to the nation by virtue of mass production. Recoupment is realized by the user in the market place and the nation by much wider spread diffusion. If the program were to recoup funds by entering in as a third party to industry--academia relationships would surely significantly delay the time when these needed capabilities would be available to the public as well as complicate the decision on the program appropriation and its role in the business community. However, industrial users of our resources always pay the full cost of their use--to that extent, we recoup the costs of providing use of our products to the private sector.

PROPHET COMPUTER NETWORK

Question: For example, the PROPHET Computer Network seems to be getting some use from industry. How much did you invest in this project--and how much are you getting back?

Answer: The PROPHET Computer Network was developed as a form of research assistance to academic based biomedical scientists. PROPHET is now used by over 700 research scientists at approximately 40 sites throughout the country.

As PROPHET's unique capabilities developed other government agencies as well as industrial groups applied for access to the Network. However, the bulk of the use continues to be by the academic research workers for whom the Network was initially developed. Thus out of approximately 40 groups of investigators now using the Network, three groups are industrially based.

The industrial users of the PROPHET Network, unlike the academic users, are not subsidized and pay the full cost of their terminal equipment acquistion, telecommunications, central processor usage and software support. In FY 1981 and 1982 the Biotechnology Resources Program, of the Division of Research Resources, is investing approximately $1.4 million per year in support of the PROPHET Network. In calendar year 1982 we project that the contributions from the three industrial users will exceed $120,000.

The industrial users of the PROPHET Network have contributed much more than monetary support to the network. The industrial users have developed software which they have made available to the entire user community through the Network. In particular the industrial users have made significant scientific and programming contributions in areas such as quantitative structure activity relations and pharmacokinetic analysis. It is impossible to put a price on such contributions when multiplied by its impact on the entire PROPHET academic, government, as well as industrial user base.

The PROPHET System has also had a commercial "spin-off" in the RS-1 computer programs now being marketed by the Bolt Beranek and Newman Corporation.

As the PROPHET Network becomes utilized by larger numbers of research scientists its economy of scale will become increasingly greater. PROPHET's software development and dissemination is driven by the scientific community which uses the Network and incorporates the contributions of its users, including industrial contributions as indicated above. This pooling of expertise and sharing of costly software development ensures that each scientist has available the newest and most efficient software tools and methods, and avoids costly "reinventing of the wheel." The PROPHET Network, with its scientific user community which encompasses a rich and diverse set of disciplines, demonstrates the benefits of collaboration among government, academic and industrial interests and may provide a model for future cooperative endeavors.

AUTOMATED MASS SPECTROMETER

Question: What is the status of your automated mass spectrometer project at Los Alamos, New Mexico?

Answer: The Biotechnology Resources Program has received an application which has been recommended for funding from Dr. L. Scott Cram of the Los Alamos National Laboratory for support of a National Flow Cytometry and Sorting Resource. The application was recommended for approval with a high merit rating; funding decisions will not be made until after final actions on the 1982 budget are completed. However, the Program has no mass spectrometry project (*per se*) from Los Alamos.

PRIMATE SHORTAGES

Question: Several years ago there was a shortage of rhesus monkeys--and you wanted to do some breeding of primates on your own. What is the status of this effort?

Answer: The severe shortage of rhesus monkeys, which developed in the mid 1970s, mandated that this species be domestically bred to meet the requirements of the biomedical community. The Division of Research Resources currently has two contracts which produce primates for extramural NIH research use. Approximately 1,400 rhesus females and 100 cynomolgus (a related species) females are in these breeding colonies. These 1,400 rhesus female breeders are producing aproximately 500 new rhesus monkeys per year.

Question: Is there still a shortage?

Answer: Within the extramural community, the success of these contracts has resulted in reducing the shortage to a few certain age and weight ranges of animals. These shortage areas include three to five year olds of either sex in the four to six kilogram weight range; five to ten year old breeders of either sex; and males in the twelve to twenty year old range.

TRAINING IN LABORATORY ANIMAL MEDICINE

Question: Why do you need to fund the training of veterinarians when it seems to be a popular occupation already?

Answer: We do not support training for the veterinary degree. Veterinary medicine is a clinical speciality which generally emphasizes domestic and companion animal problems. Our training programs provide postdoctoral training in laboratory animal medicine. Such training is intended to prepare individuals to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepared to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as a member of a research team.

It is true that there are many well-paying opportunities for new veterinary graduates. It is regarded as unlikely that they would choose an additional 2-3 year period of expensive training for the opportunity of a lower-paying research position in an academic setting without some stipend support of their graduate training. Since such individuals are a critical component of the nation's biomedical research effort, this is regarded as a worthwhile investment.

PRIMATE RESEARCH

Question: I noted that FDA has approved a new vaccine for hepatitis B which was produced by Merck, Sharp and Dohme. I understand that the government also has an extenstive hepatitis research program. To what extent are chimpanzees used for this research?

Answer: Chimpanzees are vital for continued hepatitis research as well as for research in other areas such as cancer research, reproductive research, and genetic engineering. The chimpanzee, because of its biological similarities to man, is the only animal model suitable for developing and testing vaccines to hepatitis B and Non-A Non-B. As a result of research in chimpanzees, the first hepatitis B vaccine was released last year. Approximately 50 new chimpanzees per year will be required to develop new vaccines and to safety test each new vaccine lot before it is given to humans. Chimpanzees are also essential to show that therapeutic products prepared from human blood are free of hepatitis contamination.

Question: I'm concerned about supplies of this animal. Have you projected future needs for chimpanzees?

Answer: Yes, we have projected the future need for chimpanzees through the efforts of a Chimpanzee Task Force, which has been formed as a subgroup of our Interagency Primate Steering Committee.

Question: How many chimpanzees will be needed for continued hepatitis research?

Answer: About 50 new chimpanzees per year will be needed for continued hepatitis research.

Question: Will other disciplines also need animals and, if so, how many?

Answer: Yes. Chimpanzees, because of their biological similarities to man, provide an excellent animal model for research in areas such as cancer research, reproductive biology, and genetic engineering, among others. Currently, we estimate the demand to be approximately 20 to 50 new chimpanzees per year.

Question: In what areas?

Answer: Chimpanzees will be used primarily for testing such new genetic engineering products as human growth hormone and interferon. These animals are also useful in areas like monoclonal antibody therapy, and long-term toxicity, reproductive biology, learning behavior, addiction, chronic and degenerative diseases, and other research areas.

Question: Where will these animals come from?

Answer: These new animals must be produced in domestic breeding colonies. They are nearly impossible to import because they are considered to be a threatened species, and most countries do not export chimpanzees. Like other important primates used in research, chimpanzees will have to be bred domestically.

Question: Will adequate supplies of the animals be available? Please explain.

Answer: Currently, we do have an adequate supply. Future research will probably require large numbers of chimpanzees. Chimpanzee breeding is expensive since their generation time is 10-12 years. At the present, the domestic breeding colonies are receiving short-term support through project grants and contracts. This situation is not conducive to a stable long-term national production. Under present methods some colonies will be forced to reduce their breeding efforts. Another difficulty is that the main demand is for infant chimpanzees, but as they grow older, particularly during the interval before they can be used for breeding, research use diminishes and support is inadequate. Finding new uses for these young animals may lead to adequate support, and therefore, may increase the cost-effectiveness of breeding chimpanzees.

Longer term supplies are less certain, since the principal current uses of chimpanzees require either infants (for research) or adults (for breeding). Supporting chimpanzees prior to their use as breeders is very expensive.

Question: What is the federal government, and NIH in particular, doing about these problems?

Answer: The Interagency Primate Steering Committee's Chimpanzee Task Force is studying these problems. The National Institute of

Allergy and Infectious Diseases, through an intra-agency agreement with the Food and Drug Administration, is currently providing support to New Mexico State University for hepatitis research at the Holloman Air Force Base chimpanzee colony in New Mexico. This colony consists of 360 chimpanzees used largely for hepatitis research, and represents a third of the total national supply of chimpanzees.

Currently, the Division of Research Resources is the only NIH component that provides direct support specifically for chimpanzee breeding to meet the requirements of the extramural research community. DRR supports chimpanzee breeding at the Yerkes Primate Research Center in Atlanta, with the animals destined for research purposes at Yerkes and the other six Primate Research Centers.

Question: Do you believe that the federal government should address this question more directly?

Answer: In view of the facts that chimpanzees are a threatened and irreplaceable resource, and that adequate supplies of these animals must be available for research, federal support is very important. The Division of Research Resources already has programs to insure adequate supplies of other primates such as rhesus monkeys, and, as such, it would seem appropriate for the NIH, through the Division of Research Resources to assist with maintenance and breeding programs for chimpanzees.

IMPROVEMENT OF ANIMAL FACILITIES

Question: I note that government grants to improve animal facilities have diminished dramatically in the last few years. Does this mean that facilities are now adequate?

Answer: Animal facilities remain suboptimal. For example, the seven NIH Regional Primate Research Centers have been in existence for 20 years; a survey of their facilities in 1979 revealed facility maintenance and renovation needs costing about $11,000,000. Similarly, a National Cancer Institute survey of its Centers in 1979 revealed animal facility improvement needs totaling $34,000,000; and a survey completed by the National Academy of Science, Institute of Laboratory Animal Resources in 1978 reported animal facility repairs and renovation needs nationwide in excess of $350,000,000. Almost none of these reported needs have been met. Restoring animal facilities to the optimum recommendations of the NIH Guide for Laboratory Animal Care and Use would require many institutions to raise from $2 million to over $5 million each for facility renovation (improvement) or replacement. However, given the many demands on Federal funds, it seems inevitable that the research institutions will need to rely heavily on private sources for such funds.

MINORITY BIOMEDICAL RESEARCH SUPPORT (MBS) PROGRAM

Question: What plans does the Research Resources Division have to comply with the President's initiative to assist traditionally minority institutions?

Answer: In light of the President's initiative to assist traditionally minority institutions, the Division of Research Resources is continuing to provide support to the Minority Biomedical Research Support (MBS) Program. In addition, during the past two years, DRR has developed a plan to have all the DRR programs participate in providing additional opportunities in biomedical research for minority institutions. The Biotechnology Resources Branch collaborated with the MBS Program to make PROPHET (an interactive, graphic-based computer system) available to minority institutions through the MBS Program. There are now 5 MBS institutions participating in that program. A second effort was begun in Fiscal Year 1981 when the General Clinical Research Centers Program and the MBS Program cofunded a grant to Meharry Medical College to assist them in the development of their clinical research capability. This is an ongoing activity which we will continue to support through both programs. A third initiative is being developed in Fiscal Year 1982 whereby animal resource improvement grants are being negotiated with two minority institutions. The Animal Resources Branch, the MBS Program and 2 other Institutes at NIH have agreed to cofund these animal facility improvement grants at the two historically black institutions. Through the Biomedical Research Support Program, all of the MBS institutions are provided an opportunity to participate in the Minority High School Summer Research Apprenticeship Program.

Question: What role will the Minority Biomedical Support Program play?

Answer: We expect that the support for historically black colleges through the MBS Program will continue at a level of about 60% of the total program budget. In 1981 these institutions were awarded $14.4 million through the MBS Program. We expect that this level will be maintained.

We also have a responsibility to provide opportunities to other minorities, and to blacks who happen to be enrolled in large numbers at non-black institutions. Therefore, we intend to maintain a balance in the program to provide support for both groups of institutions and all minorities presently participating.

GENERAL CLINICAL RESEARCH CENTERS

Question: In Fiscal Year 1982, you were to reduce the number of General Clinical Research Centers you were supporting. How many such Centers are you presently supporting--and what has been the effect of this cutback?

Answer: The General Clinical Research Centers Program presently supports 71 Centers. Four Centers have received phase-out budgets since Fiscal Year 1980, resulting in a loss of 25 research beds and approximately 4,000 research outpatient visits. In Fiscal Year 1980 these four Centers were the sites of 134 research projects, carried out by 116 investigators, and resulting in 289 scientific publications to date.

Question: Do you plan any further cutbacks of the Centers program?

Answer: The 1983 budget provides for six fewer Centers in 1983 than in 1982. A determination of which centers are to be closed will be made on the basis of peer review conducted during the year. Centers will be assigned priority scores according to scientific and programmatic merit. With the assistance of the National Advisory Research Resources Council, we will consider all competing centers and determine a final prioritized ranking for FY 1983 funds. It is from this final ranking that we will make the determination as to which centers are to be terminated in 1983. In addition, we have reduced the term of the center supported Clinical Associate Physicians program from three years to two.

Question: Why can't the private sector pick-up more of the costs of supporting these Centers?

Answer: The General Clinical Research Center program has been designed to support research beds costs which are not reimbursed by third party insurance carriers or by industry. Private sources already subsidize the operation of Centers to a substantial extent. The program policy provides that for ordinary patient care, patients or their insurance carriers pay. Savings from this source offset more than $15 million in program costs in Fiscal Year 1981. In addition, GCRC funds do not compensate the institutions for all the costs of relinquishing facilities to research activities; as a result, the institutions are cost-sharing significantly in these grants. Industry sources already pay for the costs of industry-initiated projects which are conducted on the Centers. Moreover, investigators using the Centers already receive substantial support from more than 1500 grants from industry and private foundations.

MINORITY BIOMEDICAL RESEARCH SUPPORT PROGRAM

Question: The Minority Biomedical Support Program is NIH's major activity concerned with improving the biomedical research capability of minority institutions and encouraging more minority students and faculty members to be involved in health related research. What is the future of this Program?

Answer: The Division is committed to continuing this program at the requested level of $18.5 million for 1983 and maintaining the commitments in future years as the need is justified. At the present time we have several applications approved for funding in-house and we anticipate receiving several new applications. A short-term evaluation is being undertaken in Fiscal Year 1982 which will give us the necessary information to establish priorities and associated funding requirements for this program. It is clear that the program is doing well. It is a valuable program for participating institutions involved, and the Division is committed to continuing the program as long as this need remains.

Question: To what extent has this program suffered cutbacks in the past fiscal year, and what support will it receive for FY 1983?

Answer: Athough the MBS Program in 1982 was reduced $787,000 below the 1981 level, we will continue to fund 74 grants in 1982 by negotiating all awards downward by an average of four percent. The 1983 budget request of $18.5 million will allow for the support of 68 Minority Biomedical Research Support grants.

REGIONAL PRIMATE CENTERS

Question: What is the status of the seven Regional Primate Research Centers located around the country?

Answer: The seven Regional Primate Research Centers continue to be highly active and productive. The Centers constitute a major national scientific resource for nonhuman primate research aimed at the solution of human health problems. Through their use of various species of primates and the specialized facilities of the Centers, the 150 core staff scientists and 550 affiliated scientists from outside institutions are carrying out investigations in numerous biomedical areas, including reproductive biology, infectious diseases, neurosciences, toxicology, nutrition, environmental health and the behavioral sciences. Approximately 700 scientific publications resulted from this work during the past year.

TRAINING IN LABORATORY ANIMAL MEDICINE

Question: Have you been able to continue the training of post doctoral level investigators in laboratory animal medicine?

Answer: Yes, on a modest level. There are 8 currently active institutional training awards with a total of 28 funded trainee positions. In addition to the institutional programs, one individual postdoctoral fellowship was active at the end of the fiscal year. Since the average training period is two and one-half years, there are usually 8-10 graduates per year. Currently available figures indicate that 169 trainees and fellows have completed training since the inception of the training grants and fellowships in laboratory animal science and medicine. Fifty-nine (59) of these are employed by medical schools and 64 by other academic, research or govenmental organizations. The majority (104) are serving as directors or staff members of a vivarium; 50 are engaged in teaching and research or are obtaining additional training; and 15 are in public health, private practice or are retired. Retention in the field of laboratory animal medicine has been excellent, emphasizing the career orientation provided by the training and the continuing need and opportunities available for such individuals.

The following figures from the 1979 Survey of Laboratory Animal Facilities and Resources conducted by the Institute of Laboratory Animal Resources, National Academy of Sciences, demonstrate the continuing shortage of trained specialists in this area:

	FTEs Employed	FTEs Unfilled	Additional FTEs Needed by 1983
Grant Eligible Institutions	321.5	111.7	239.1
All Organizations*	525.9	165.9	350.5

*Includes Federal agencies, industry, and grant eligible institutions.

The above figures are considered reasonably current in terms of today's need since we are aware of numerous funded but unfilled positions for well-trained specialists. Specific areas of the overall shortage which are of special Federal policy concern relate to animal welfare requirements (Public Law 89-544 as amended by Public Laws 91-579 and 94-279).

PRIMATE BREEDING IN THE PRIVATE SECTOR

Question: Why isn't the private sector taking over this support?

Answer: The private sector has been unwilling to bear the rather high costs associated with the initial establishment of primate breeding colonies without cost-sharing or supplemental funding arrangements with the federal government. Although no monetary savings would be anticipated, we believe that it would be desirable for private enterprise to take over routine primate breeding for the biomedical community. An exception would be for the highly specialized needs of the DRR-sponsored Primate Research Centers, where breeding on location at each Center will continue to be necessary.

BIOMEDICAL RESEARCH SUPPORT PROGRAM (BRSP)

Question: Under existing fiscal constraints, to what degree were you able to strengthen your Biomedical Research Support Program (BRSP) over the past year?

Answer: Recognizing the need to maintain a vigorous and healthy Biomedical Research Support Grant Program and to ensure that the institutions most heavily engaged in biomedical research continue to receive awards commensurate with their demonstrated biomedical research capability, two key administrative changes have been instituted: The formula for computing the size of the awards to eligible institutions has been adjusted to stop the disproportional decline in the size of awards to institutions most actively engaged in biomedical research. The former static formula has been replaced with one that reflects and compensates for yearly changes in the number of eligible institutions and the dollar volume of Public Health Service research grants awarded to them. In addition, the eligibility threshold to gain entrance into the Program has been raised from $200,000 to $500,000, effective in FY 1983. This criteria ensures that the eligibility threshold continues to reflect the same level of heavy engagement in health-related research by grantee institutions as it did in the mid-1970's. Also, it has been decided that the eligibility threshold for future years BRSG's will be subject to adjustment each year at a level commensurate with the total NIH dollar availability for research grants.

Question: What have you done about defining the goals of the Program?

Answer: The objective of the BRSG Program has been clearly defined and set forth in our Program Guidelines as follows:

> "To strengthen and enhance the research environment of institutions heavily engaged in health-related research through the use of flexible funds and local decision making which enable them to more efficiently and effectively conduct their biomedical research programs."

This basic objective of the Biomedical Research Support Grant (BRSG), as established by legislative history and intent, is to extend opportunity and responsiblity to the scientific/administrative leadership at the institutional level for making specific on-site allocations for biomedical research purposes. This is to assure that a portion of the total NIH funds for biomedical research utilizes local decision making, allowing for appropriate internal balancing of needs as well as early recognition and development of emergent research concepts, techniques and talents.

This statement of objectives has been conveyed to the General Accounting Office as they previously requested.

LIVE ANIMALS IN RESEARCH

Question: To what extent are you involved in the search to find more non-animal alternatives that could some day replace and reduce the need for many animals now used in biomedical research?

Answer: The Division is planning a series of workshops to determine both the opportunities for, and limitations of using lower organisms, tissues/cells in culture, and mathematical and computer systems as potential biomedical research models.

The Division is also examining new developments which we are supporting in computer systems, instrumentation, and biological models which may lead to replacement or reduction in the use of higher animals in biomedical research. Specific examples are:

- acquisition, maintenance, and supply of sea urchins, squid, and octopi to the biomedical research community.
- Computer systems essential to positron-emission trans-axial tomography (PETT), biostatistical methodologies, neuroanatomical image processing, ultrasonic attenuation tomography, etc.
- Development of instrumentation having broad applicability to biomedical research, e.g., high voltage electron microscopy, mass spectrometry, nuclear magnetic resonance spectroscopy, and electron spin resonance spectroscopy.

At the same time, research is being supported to discover and develop new and more effective uses of animals in research seeking to improve and protect human health.

Question: Why is there a search on for so-called nonanimal alternatives?

Answer: Animals used in research require costly care and space. They carry the potential for introducing variables that must be controlled. The Division continues to seek and explore opportunities for the development of nonanimal alternatives if they can offer simpler, more effective models for biomedical research that may result in more useful scientific data being obtained in less time, and at a reduced cost.

GENERAL CLINICAL RESEARCH CENTERS

Question: It is interesting that even though you plan to reduce the number of General Clinical Research Centers from 71 to 65, you propose increased funding of some $3 million in this area. What accounts for this seeming anomaly?

Answer: This anomaly is a result of the increased costs of hospital care and clinical research. A 1982 report in *Hospitals* from the American Hospital Association indicates that community hospital expenses increased 17.9 percent between September 1980 and September 1981. Using a more conservative estimate of 14.3 percent increase between Fiscal Year 1982 and Fiscal Year 1983 we estimate that we will be able to support only 65 Centers in Fiscal Year 1983, despite a $3 million increase in the budget.

Question: Why is it you believe that there may be increased demand for General Clinical Research Center beds in Fiscal Year 1983?

Answer: The expected increased demand for General Clinical Research Center beds is attributable directly to the increase in clinical research initiatives in areas such as diabetes. For example, in 1979 the patient days for diabetes research cost $6.7 million or 13.3 percent of the Clinical Research budget, while in 1981, patient days for diabetes research beds cost the program $12.7 million or 21 percent of the program's budget. We anticipate this increased demand to continue as more investigators attempt to transfer the knowledge that has been gained from basic research into clinical applications.

EXTRAMURAL GRANT SUPPORT

Question: We are advised that you did not fund any research project grants in FY 1982 and that all of the extramural grant support goes into research centers and other research mechanisms. If this is true, what is the reason for it?

Answer: It is true that we are not funding any research project grants in 1982. However, the Division's mission is to strengthen and enhance the research environments of institutions engaged in health-related research by developing and supporting a wide variety of essential research resources. The research project grant mechanism at NIH is a mechanism to provide support to investigator-inititiated research projects, while the centers and other research mechanisms are categories designed for broader institutional support. As a result, all of RR's extramural activities are carried out through these two mechanisms.

Nevertheless, the Division provides support to individual investigators through our awards for institutional support. For example, grants for Minority Biomedical Research Support, although made to institutions, include funds for research projects (called subprojects in the grant). These are analogous to the support provided to investigators in program project grants. Also Biomedical Research Support Grants funds support pilot research directly. Finally, the DRR supports Resource-Related Research Project Grants for research and development of resources.

Question: Will the DRR fund any research project grants in FY 1983?

Answer: No. DRR will continue to fund only research centers and other research grants in 1983.

MINORITY APPRENTICESHIP PROGRAM

Question: Why is DRR running a Minority Apprenticeship Program for high schoolers during the summer?

Answer: In 1980, the Director, Office of Science and Technology Policy requested that the seven federal agencies supporting basic research allocate some of their funds to be used by non-federal laboratories to hire minority high school students for summer employment. The DRR was assigned the responsibility for this activity on behalf of the NIH, by the Office of the Director.

Question: How much is this costing-- and what useful purpose does it serve?

Answer: The basic objective continues to be one of providing a short term but meaningful experience in various aspects of health-related research in expectation that some of the apprentices will decide to pursue careers in research related to health. In FY 1981, 666 students were supported at a cost of $1 million. In FY 1982, we will support 640 students at a cost of $960,000. The President's FY 1983 request of $1 million will support 666 students.

Question: What do the "Apprentices" do during their summer internship?

Answer: The apprentices work in research laboratories with research faculty as their preceptors for an eight week period. They learn relevant laboratory techniques; they learn to work and cooperate with members of a research team; and they are exposed to the realities of a college environment.

One such apprentice characterized the experience in the following manner--"This program is excellent because it gives one practical experience in the laboratory and the chance to learn about the sciences. It is an honor to work with people who are not only greatly respected in their fields, but also friendly and efficient in their work."

STATUS OF MBS PROGRAM

Question: Bring us up-to-date on the Minority Biomedical Support Program. How well is it doing?

Answer: The overall goal of the MBS Program is to increase the number of minority scientists engaged in biomedical research. While an absolute measure towards attaining this goal must await a comprehensive review of the MBS Program, nationally there are indications that it is being successful. For example, in FY 1979, a total of 474 MBS students graduated with a baccalaureate degree with 131 of these students continuing their studies in medical school and 130 continuing their studies in graduate schools. The MBS students entering medical school represented 8.5% of the minority students enrolled in first year classes in U.S. medical schools in the 1980-81 academic year. A specific example can be seen by focusing on Knoxville College which is a small private, liberal arts college of about 500 students. Since the initiation of its MBS Program in 1973, a total of 27 students graduating with a B.S. degree in biology pursued advanced degree programs. Eleven of the 27 (41%) were MBS participants. Three MBS students entered medical school; two entered dental school; one entered a school of medical technology; and five entered graduate school. One of these latter students recently received his Ph.D. from the University of

Tennessee and is currently carrying out post-doctoral studies at the University of California, Irvine. Over the same period a total of 17 students graduated with a B.S. degree from the Departments of Chemistry and Mathematics and entered a professional or graduate degree program. Thirteen of these students (76%) were MBS participants of which one entered medical school, and twelve entered graduate school.

In terms of faculty participants the program has seen an increase in absolute numbers and a concomitant increase in productivity. Approximately 200 faculty participated in the MBS Program in 1972 while that number was above 600 in FY 1980. In 1974 only 15% of the faculty published at least one paper. This increased to 83% in 1980. Similarly, faculty presentation of research papers increased from 20% in 1974 to about 69% in 1980.

Although the program is beginning to make an impact in the underrepresentation of minorities in biomedical research, there are still relatively few in the mainstream. All of the investigators are young and are now facing stiff competition with experienced investigators for limited research funds.

MINORITY BIOMEDICAL RESEARCH SUPPORT (MBS) PROGRAM

Question: The Minority Biomedical Support Program has had an impact on Florida A&M University in Tallahassee. I am concerned that the emphasis might be on the decline. $2 million was restored to the program budget--is that $2 million reflected in the 1983 budget?

Answer: No, that $2 million is not reflected in the 1983 budget.

The $2 million you are referring to is the amount that the administration proposed for rescission in 1981, but that the Congress restored. This Congressional action raised the 1981 funding level of the MBS program $2 million to $18.8 million. However, the 1982 level of $18.1 million was derived from the President's 1981 proposed rescission level of $16.8 million, which did not reflect the restored $2 million. The 1983 President's budget request of $18.5 million was derived from the 1982 level of $18.1 million. As a result, the $2 million restored in the 1981 budget is not reflected in the 1983 budget.

Question: Is there a proper increase for inflation in the 1983 budget?

Answer: Within the budget level designated for the Division of Research Resources, the Minority Biomedical Research Support program has an increase of $443,000, or 2.5 percent, over the 1982 level. This level of funding will enable us to fund 68 Minority Biomedical Research Support grants, six fewer than in 1982. In spite of the $443,000 increase, the increased cost of conducting biomedical research has decreased our purchasing power, reducing the number of MBS grants we can suppport.

Question: In 1980 and 1981, there were 80 total grants made in the Minority Biomedical Support Program. The total for 1983 reflects a decrease to 68, why is a decrease anticipated?

Answer: Increases in the cost of doing research make it difficult to support more than the 68 grants reflected in the President's Budget request. We expect that, through attrition, some of the programs currently receiving support will no longer be in contention for support in 1983. Nevertheless, as a result of increased research costs, we will only be able to support those noncompeting and competing renewal applications that receive the highest priority scores in their peer review. We do not plan to support any new awards within the 1983 budget.

Question: Did you have a decline in the number of black institutions applying for MBS funds, if so why?

Answer: There has not been a decline in the number of applications from black institutions. However, there is a tendency for the smaller black institutions to seek support for programs that are not as research oriented, but those that fit more within their primary mission of education. Several workshops were conducted (involving 350 faculty) to address this problem in 1979-80. There has been an increase in numbers of applications from these institutions since the workshops. In 1980, 30 MBS applications, or 52 percent of the total applications received, were from black institutions. In 1982 the percentage has increased to 57 percent of the total, or 36 applications.

UNFUNDED GRANT APPLICATIONS

Question: Do you have any "approved" but unfunded grant requests in the Division presently? How much does this represent?

Answer: We currently have 18 approved unfunded Minority Biomedical Research Support grant applications in-house (4 new and 14 supplemental) totaling $2.2 million for their first year and $5.1 million for their total 3 year requests.

Within the entire Division, we currently have over $58 million worth of approved, unfunded applications. For the rest of the Division, the approved, unfunded applications currently in-house amount to $3.9 million in the Clinical Research Program, $11.9 million in the Biotechnology Research Program, $5 million in the Laboratory Animal Sciences and Primate Research Program, and $35.3 million in the Shared Instrument Grant Program of the Biomedical Research Support Program.

GOALS OF THE MBS PROGRAM

Question: Has the Minority Biomedical Support program met its goals? If not, how do you propose to meet the goals of the program?

Answer: The overall goal of the MBS Program is to increase the number of minority scientists engaged in biomedical research. While an absolute measure towards attaining this goal must await a comprehensive evaluation of the MBS Program, there are indications that it is being successful. For example, there have been nearly 4,600 minority students who have graduated from institutions with MBS programs. About 50 percent of these students have gone on to pursue advanced degrees in health professions. Another 40 percent have gone primarily to graduate school to pursue the Ph.D. degree in biomedical sciences. Most of the others have entered health science careers at the paraprofessional level.

The MBS program has been successful enough in improving the research capabilities of minority institutions that eight institutions participating in the program have entered the mainstream of biomedical research with investigators successfully competing for, and receiving, research project grant support. In addition, 14 MBS institutions have been successful enough in their research endeavors to attain Biomedical Research Support Grant eligibility.

As a result of the scientific excellence achieved by MBS participants in recent years, it had been suggested that the name of the program be changed to the Minority Biomedical Research Support program. The addition of the word "Research" in the title is to recognize the fact that the program has evolved to the point that significant high quality research is being conducted. This name change has been made official, and now provides a much more accurate description of the program's activities.

We intend to complete our evaluation study of the MBS program early in 1983, and hope to have the results of that study by the time of next year's appropriation's hearings.

BLACK COLLEGES

Question: How many black institutions are involved in the MBS Program? Do you consider this total "acceptable"?

Answer: We presently have 48 historically black institutions supported through the MBS Program involving a total of $14.4 million. We also have a responsibility to provide opportunities to other minorities and blacks, who happen to be enrolled in large numbers at non-black institutions. Therefore, we intend to keep a balance in the program to provide support for both groups of institutions and all minorities presently participating.

JOHN E. FOGARTY CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

STATEMENT OF DR. CLAUDE J. M. LENFANT, DIRECTOR

ACCOMPANIED BY:

WILLIAM DOAK, EXECUTIVE OFFICER

THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Dr. MALONE. Mr. Chairman, I am being joined by Dr. Claude Lenfant, Director of the Fogarty International Center. And with him is Mr. William Doak, the Executive Officer, at the table.

Senator RUDMAN. Doctor, thank you very much.

We have your statement, I believe, and we would like to proceed with a brief overview. And we will have a few questions for you and your colleagues.

SUMMARY STATEMENT

Dr. LENFANT. Thank you, Mr. Chairman.

I would like to summarize my statement by making some brief comments about the overall goals of our programs.

Senator RUDMAN. Doctor, if you could move the microphone slightly closer, I think it would be easier for the stenographer and certainly for us up here.

Dr. LENFANT. The Fogarty International Center is the NIH focal point for international activities and for research conducted abroad. We discharge our responsibility through four programs which are described in detail in my statement.

The common aim of all of our programs is to assure better scientific communication and to foster exchange of information and data between our scientists and researchers in foreign countries.

Our activities are an integral part of the overall NIH mission. Scientific communication with the rest of the world and access to foreign research capabilities and discoveries benefit nearly all NIH research programs.

There are, Mr. Chairman, numerous examples showing that foreign participation in our research has speeded up our own advances in biomedical research and in prevention, control, and treatment of diseases.

To underline the significance and importance of our linkage with foreign research communities, if you permit me, Mr. Chairman, I would like to read a statement which was recently published in an evaluation report of the Fulbright program:

> A quarter of a century ago, about two-thirds of the world's scientific activities were judged to take place in the United States. Today, the figure is closer to one-third in view of the major progress in other countries.

Thank you, Mr. Chairman. I would be glad to answer questions.

EFFECT OF CONTINUING RESOLUTION

Senator RUDMAN. Doctor, I will ask you the same question that I have asked the other witnesses. First, two common questions. What has been the effect of the 1982 Continuing Resolution as it was implemented by your particular Institute?

Dr. LENFANT. As you know, Mr. Chairman, one of the major outlays of our expenditures is for our fellowship programs. Because of the reduction in funds, we have been obliged to do two things. First, we will be awarding fewer new fellowships.

In addition, whereas in the past, fellows were allowed to apply for extensions as long as 1 year, this year, we have been obliged to reduce that to a 6-month maximum extension.

RESPONSE TO BUDGET CONSTRAINTS

Senator RUDMAN. In light of those constraints and others, what efforts have you undertaken in this year's budget which does have a fairly respectable increase in it, but nevertheless, what are you able to do in terms of administrative overhead within your own agency, your own Institute?

Dr. LENFANT. We have reduced or eliminated a number of the expenses which we previously had; such as for publications. We have also reduced the number of conferences that we are supporting. We also have decreased some of the expenditures we had in the past in our scholars-in-residence program.

FLU VIRUS CONFERENCE

Senator RUDMAN. We note you are planning the flu virus conference, I believe, in the People's Republic of China; is that correct?

Dr. LENFANT. As part of our international issues study program, we are going to hold a conference on measles next month. I trust that is the one you are referring to. That conference will, indeed, have some participants from the People's Republic of China.

Senator RUDMAN. Well, you are holding one, am I correct, in the People's Republic of China? Is that correct? Is that where you are holding it? Where is it being held?

Mr. DOAK. If the grant application we have received is approved that conference would be held in China.

Senator RUDMAN. It is being held in China?

Mr. DOAK. Yes.

Senator RUDMAN. Could you tell us how many people from Fogarty will attend, and exclusive of their normal salaries how much this will cost?

Dr. LENFANT. Excuse me, Mr. Chairman, but I believe there may be some confusion regarding the sponsorship of this conference.

Senator RUDMAN. Mr. Doak, which conference are you referring to? Because I am more confused than both of you. Is there a conference being held in the People's Republic of China under the sponsorship of the Fogarty studying flu viruses?

Dr. LENFANT. The conference is not being sponsored by the Fogarty International Center.

Senator RUDMAN. What is your answer, Mr. Doak?

Mr. Doak, you can pull that microphone over to you. I am asking you a question.

Mr. DOAK. The Fogarty International Center has received a conference grant application to provide partial support for an international congress in the People's Republic of China. I believe the location was selected because Asia is the source of most new strains of influenza.

Senator RUDMAN. Let me read to you and Dr. Lenfant so you both understand what I am referring to from the backup which you have supplied to us. And this may be a perfectly proper exercise of your funds; I am not saying it is not. I am just trying to find out what is going on since that is allegedly one of the purposes of these hearings.

It says: "The conference and seminar program provides a forum at the international level for discussion of advances in the health sciences, biomedical and behavioral science," and so forth.

Then, it says, "Examples include a workshop on chromosomes in leukemia, the influence of environment on leukemia and lymphoma," and a conference on another medical term which I will not botch up, "and neuromuscular functions. The conferences scheduled for 1983 include a workshop on the origins of pandemic influence of viruses. This conference will be held in China and will permit extensive involvement by scientists from Asia, the area of the world where new strains of flu virus evolve."

My question is: Is this conference being held under the aegis of the Fogarty or is someone else sponsoring?

Dr. LENFANT. Several groups will sponsor the conference, Mr. Chairman. A conference grant application has been submitted to the Fogarty International Center requesting funds for partial support of such a conference next year in the People's Republic of China. That application has not yet been reviewed nor have funds been committed to that activity. In any event the Fogarty International Center would not be sponsoring the conference. The sponsors are probably organizations concerned with infectious or viral diseases.

Senator RUDMAN. Which would sponsor it, but would apply for funds?

Dr. LENFANT. Exactly.

Senator RUDMAN. All right.

Dr. LENFANT. I apologize for the confusion.

FUNDS FOR FLU VIRUS CONFERENCE

Senator RUDMAN. All right; fine.

Now, I will recast my question. Could someone tell me how much money is being requested by the independent sponsoring medical organization for a flu virus conference to be held in the People's Republic of China?

Dr. LENFANT. The request is for $39,000. However, the Fogarty International Center would pay only a fraction of this amount if the application is approved.

Last year, Mr. Chairman, the NIH as a whole spent $319,000 for conferences held abroad. The Fogarty International Center's contribution was $120,000.

ATTENDEES AT FLU VIRUS CONFERENCE

Senator RUDMAN. Could you tell me if this conference is in fact held and if it is approved, would there be as a matter of course people who work for the Fogarty who would attend this conference in their official capacity?

Dr. LENFANT. No one from the Fogarty International Center will go, but bench scientists might apply and be supported through our funds.

GORGAS MEMORIAL LABORATORY

Senator RUDMAN. Dr. Lenfant, if I can speak just for a moment about the Gorgas Memorial Laboratory that studies tropical medicine, could you tell me if the Latin American countries, any of them, contribute and how much any of them contribute in percentage toward funding and maintaining of that laboratory?

Dr. LENFANT. Yes, Mr. Chairman. The contribution to the Gorgas Laboratory from the Fogarty International Center is approximately 64 percent of their budget. The contribution from the Government of Panama is about 9 percent. Other countries do not really support this laboratory. There are, however, some funds which come in from the World Health Organization and from the Pan-American Health Organization. The bulk of the support, approximately 75 precent, is from the National Institutes of Health. The balance is from the Army and Navy.

CONTRIBUTIONS TO GORGAS BY OTHER COUNTRIES

Senator RUDMAN. That was just the reason I asked the question, Dr. Lenfant. It would seem that since these particular diseases are tropical in nature, of course, the very focus of what this laboratory does, since they are certainly indigenous to those countries in a greater way than to our country, would it be unreasonable to assume that some of these Latin American countries might contribute somewhat more to the support of this particular laboratory and if not why not?

Has anybody asked them to?

Dr. LENFANT. The Government of Panama, where the laboratory is located, supports the laboratory by providing the facilities, utilities, and other contingencies which are necessary for the function of the laboratory.

I should say, Mr. Chairman, that the United States is not exempt from some of the diseases studied by the Gorgas Laboratory, although they are indeed prevalent in that part of the world. The laboratory has a surveillance function vis-a-vis epidemics and in that way is extremely important to our research program.

In addition, the Armed Forces of the United States and other American citizens often are in parts of the world where tropical diseases are prevalent; therefore, any study that we pursue on these diseases benefits us.

Senator RUDMAN. I think those are very valid points, Dr. Lenfant. Certainly, the Armed Forces have great concerns about various tropical diseases. And the contribution Panama makes is substantial.

It just seems to me—and I am only one Senator—that you have a program that is devoted to studying tropical diseases in the tropics; that the countries other than this one, particularly Latin American countries, some of those particularly who are rich in newly found resources, might make more of a contribution than obviously they are.

We are supporting 75 percent of this. And I am sure it is worthwhile. But it would be something that I would appreciate a more detailed answer on the record, specifically as to what efforts have been made by NIH or by the State Department if they are made otherwise to bring more participation by Latin American, Central American countries into the funding for this particular project.

Dr. LENFANT. May I, Mr. Chairman, point out that neither NIH nor the Department has anything to do with this appropriation which has been provided for by the Congress. The Department and the Fogarty International Center are used as a conduit to make that appropriation.

Mr. ITTEILAG. Senator, may I comment along those lines?

Senator RUDMAN. You certainly may, Mr. Itteilag.

Mr. ITTEILAG. As you know, the amount for the Gorgas Laboratory is set forth in the appropriation language, therefore, an appropriation's bill having been passed, we are bound by statute to spend money for that purpose.

Senator RUDMAN. We can pass new laws very quickly.

Mr. ITTEILAG. Yes, sir, you could. But the history of this particular provision is that it was imposed upon the executive branch by the Congress, and it is essentially for that reason that it remain in the appropriation's bill at this time.

Senator RUDMAN. I understand it has been static for some time, and I am sure that the people who were involved in the funding of that back in those days with that statutory language, most of them, are not here any more. And this has become a tradition. And it just goes on and on and on.

And I guess my question which seems like a very simple question—maybe it is very complicated—is that the people who handle the gift and are involved in the laboratory at least might take the time to make inquiries of their counterparts in foreign countries and say, "Would you like to help a little bit?"

That seems like a very simple thing to do. And I would still like an answer on the record as to whether or not that has ever been undertaken by anyone. And if it hasn't maybe we will find a way to do it. I am not saying that critically; I am just saying maybe that is something people ought to look at.

It is not a great deal of money, but as I go through hearings in this appropriations committee on the various subcommittees that I serve on, I have come to the conclusion we are going to have to make a great deal of conscious effort to save a great deal of money in various areas. I will not use the old cliche, but I am simply telling you, eventually, it does add up. So we would like an answer on the record for that.

PREPARED STATEMENT AND SUBMITTED QUESTIONS

Thank you very much, Dr. Lenfant, for your testimony. And please do try to answer that question for me.

We will give you other questions for the record.

[The statement and the following questions which were not asked at the hearing but were submitted for response for the record follow:]

STATEMENT OF DR. CLAUDE J. M. LENFANT

I am pleased to have the opportunity to report once again on the activities and accomplishments of the Fogarty International Center during the preceding year. As you may recall, when I spoke to you in 1981 I had been with the Center only a few months. Since then, I have gained a clearer perception of the vital role the Center plays in fostering international cooperation to extend the impact of health-related research. Through extensive contacts during the past year with scientists and officials of many countries, I have developed new insights into how the Fogarty International Center has contributed to disease prevention and health maintenance worldwide. Through such cooperation with other countries, health-related research in the U.S. also receives tangible benefits: Research funds are used more cost effectively when U.S. and foreign scientists bring complementary skills and approaches to bear on the same problem, and when scientific resources available elsewhere are not duplicated.

Drawing upon my fresh impressions and with the cooperation of the Center's staff, we have undertaken administrative and organizational changes to sharpen the focus of our activities, making them even more responsive to international health problems as well as to the needs of the NIH and other Federal agencies with goals that are similar or complementary to ours. The Center now fulfills its mission through four major programs: Advanced International Studies; International Research and Awards; International Coordination and Liaison; and Foreign Scientists Assistance.

A feature common to these programs is that they redound to the benefit of biomedical research, disease prevention and disease control in the U.S., and at the same time have a comparable impact in foreign countries. No one country has a monopoly on advances in health-related research and technology. It is, therefore, of value that the Fogarty International Center offers various supportive and administrative mechanisms for international cooperation. These mechanisms contribute to the dissemination of new knowledge and the utilization of new techniques, and they foster collaborative studies that minimize duplicative efforts and capitalize on populations or disease problems peculiar to a given geographic area.

Advanced International Studies

Since its inception, the Fogarty International Center has fostered advanced studies through its Scholars-in-Residence, and Conferences and Seminars programs. Within the past two years, a third component -- the International Issues Study-Program -- has been under development. The distinguished scientists who spend up to a year at the NIH as Scholars-in-Residence share their knowledge, skills, and ideas with each other and with NIH scientists. They often participate in collaborative research on the campus and, through conferences and seminars as well as informal exchanges, contribute to the intellectual environment at the NIH. As problems of world health change and as additional developing countries participate in scientific health-related activities, it is appropriate to examine even such successful activities as the Fogarty Scholars program, to learn whether they adequately serve current needs. Initiated during the past year and still in progress, are working groups of NIH and outside experts who are assessing the Scholars-in-Residence program. It is in no way our intention to modify aspects that have so eminently proven successful in the past, but rather to extend the usefulness of the program without sacrificing its desirable features. The working groups have been asked to consider whether the program should be modified to encompass a broader scope of disciplines (e.g., epidemiology, behavioral science), whether an effort should be made to accommodate to the schedules of scientists who cannot devote a period as long as a year as a scholar at the NIH, and whether nomination procedures could be improved to encourage wider participation in the nomination process by the NIH staff.

This year the Scholars-in-Residence program was maintained at a level deemed necessary for a critical mass; namely, 10 scholars. It is important to have enough scholars present at any given time to ensure opportunities for intellectual stimulation. For example, because leading immunochemists from Israel and the U.S. were in residence at NIH simultaneously, the scientific exchanges resulting from their presence had a profound influence on fundamental work on protective immune mechanisms.

Conferences arranged by and supported through the Conferences and Seminars program provide a forum for discussion of health-related topics and are often a stimulus to innovative research approaches to disease problems. Because Fogarty Scholars-in-Residence are encouraged to plan conferences during their sojourn at the NIH, there are close links between these two facets of the Advanced International Studies Program. During the past year, the International Conferences and Seminars program has been carefully reviewed and administrative changes undertaken to sharpen its international focus, and to make the procedures for scientific merit review of extramural applications for conference support consistent with those for other NIH grant applications.

During fiscal year 1981, the Fogarty Center contributed about 10 percent of the cost of 73 approved conferences, supporting only international aspects of the meetings. The Center also provided about one-half the support for five intramural conferences with international components. Among timely topics of particular interest were the biology of interferon and the question of use, availability, and patenting of hybridomas that produce monoclonal antibodies.

The International Issues Study-Program is designed to identify health issues of international concern and develop feasible strategies for addressing the issues. This program will both draw upon and feed into the other two components of the Advanced International Studies Program, and will obtain advice from both the NIH and outside experts. As part of the International Issues Study-Program for 1982, task forces have been organized to develop an approach that could lead to eradication of two diseases -- measles and poliomyelitis. Among the participants in the task forces are Scholars-in-Residence as well as NIH scientists, representatives from the Food and Drug Administration, the Centers for Disease Control, and other government agencies, and also from the World Health and Pan American Health Organizations. The task forces are organizing a number of scientific conferences to assess the feasibility of achieving eradication of these diseases, to identify gaps in knowledge needed to conduct an eradication program, to identify the research resources needed to facilitate eradication, and to consider possible political or socioeconomic barriers to an effective, worldwide eradication program.

International Research and Awards

To enable biomedical or behavioral scientists in various phases of their careers to expand their intellectual horizons or to engage in collaborative research in countries other than their own, the Fogarty International Center administers a variety of programs. This is a bi-directional activity that brings foreign scientists to U.S. laboratories and sends U.S. researchers to foreign scientific institutions. The International Research Fellowship Program, which predated the Fogarty Center by a decade, has been administered by the Center since 1968 and funded by it since 1970. Its value has been amply demonstrated, as I reported last year. Since then, new nominating committees have been established in Romania, Venezuela, and Zimbabwe. There is, however, concern because the nominating committees of some countries are inactive, and others do not submit adequately prepared applications or do not screen carefully the credentials of candidates they propose. These problems are now receiving attention. Efforts are also underway to encourage establishment of nominating committees in several countries, including the People's Republic of China. Under consideration is the development of a small grant program for returning fellows to facilitate reestablishment of their research in their home countries.

U.S. scientists with established reputations as researchers are eligible for Senior International Fellowships to spend up to one year in a foreign laboratory. Supported by the Fogarty International Center since 1975, this program has made 342 awards for fellows going to 32 countries. The program is now being evaluated to assess its contribution to the recipients and to the host and sending countries. France, Sweden, and Switzerland also support fellowships for U.S. scientists, but these are for scientists in the formative phases of their careers. The Fogarty International Center has administrative responsibility for these programs until the fellowship is funded by the foreign country.

The Center also contributes to the support of individual exchanges of well-qualified U.S. and foreign health scientists who wish to collaborate in research. The scientists are jointly supported through agreements the U.S. has with four Eastern European countries and France.

The Fogarty International Center is the organization through which funds are appropriated annually by the Congress to support research conducted by the Gorgas Memorial Laboratory in Panama. The research is largely addressed to prevention of diseases prevalent in the tropics, particularly in Panama and Central America, but also in the U.S.

Collaboration between the U.S. and foreign scientists is still supported in a few countries through the Special Foreign Currency Program (P.L. 480), which is administered by the Fogarty International Center. When P.L. 480 funds are depleted, this support is replaced by matching funds administered by joint boards, which have been established to review and monitor individual projects.

International Coordination and Liaison

As the focal point for international activities at the NIH, the Fogarty International Center serves as a link between foreign countries and NIH institutes and divisions, other U.S. agencies, and international organizations concerned with problems of world health. Because numerous NIH institutes (in some instances as many as 9 or 10) participate in bilateral agreements with a given country, the liaison provided by the Fogarty International Center ensures smooth coordination of complex relationships. At present there are 41 bilateral agreements with 26 countries, the most recent additions being China (1979), Greece, Kenya, Senegal, Venezuela, and Zimbabwe (1980), Kuwait and Nigeria (1981). These agreements have been of immeasurable value in reducing social and political barriers to scientific exchanges, capitalizing on unique features of local environments and resources, fostering collaborative undertakings with shared technical and professional resources and expertise, and in sharing the cost of these exchanges.

The most eloquent testimony to the effectiveness of international cooperation in contributing to disease prevention and betterment of world health is provided by the following examples of scientific investigations and accomplishments resulting from collaboration between U.S. researchers and their foreign counterparts:

Prevention of blindness is the ultimate objective of a collaborative study by scientists from the Soviet Union and the National Eye Institute. To treat glaucoma, they are studying the efficacy of a modified laser beam (Q-switch laser instrument) that generates almost no heat. The instrument was developed by Soviet scientists, and the trial is being conducted in both the Soviet Union and the U.S. The National Eye Institute has also established a research center in Hyderabad, India, to investigate nutritional blindness. This is a pervasive problem among children in nutritionally deprived regions of the world that could be prevented if more were known about suitable dietary changes.

Prevention of hypertension by dietary modification is the focus of a cooperative study by U.S. and Japanese scientists who are using a stroke-prone animal model available in Japan. The model is a spontaneously hypertensive rat that was developed at Kyoto University and is of interest in the present study because it appears to be protected against stroke when provided with a particular dietary protein.

In conclusion, I wish to reaffirm our conviction that it is essential to the scientific progress and health of the Nation to have a strong, aggressive international program in biomedical research. Such a program will enable the U.S. to capitalize on foreign discoveries to the benefit of its own research and treatment activities and avoid duplication of effort with a consequent savings in scarce resources.

The proposed budget for the Fogarty International Center for fiscal year 1983 is $10,147,000. I shall be pleased to reply to any questions.

BIOGRAPHICAL SKETCH

LENFANT, Dr. Claude J.M.
Director, Fogarty International Center, National Institutes of Health

October 12, 1928 - Paris, France

Education: 1948 - B.S., University of Rennes, France. 1956 - M.D., University of Paris, France. 1957-58 - Postdoctoral Fellow, University of Buffalo. 1958 - Postdoctoral Fellow, Columbia University.

Professional History: 1954 - Research Assistant, Centre Marie Lannelongue, Paris, France. 1955-1956 - Research Associate, Centre Marie Lannelongue. 1956-1957 - Director, Laboratory of Experimental Surgery, Centre Marie Lannelongue. 1959-1960 - Assistant Professor of Physiology, University of Lille, France. 1961-1965 - Clinical Instructor of Medicine and Physiology and Biophysics, University of Washington. 1961-1968 - Associate Director, Institute of Respiratory Physiology, and Staff Physician, Firland Sanitorium, Seattle. 1968-1971 - Associate Professor of Medicine and Physiology and Biophysics, University of Washington. 1969-1971 - Consultant, University Hospital, Seattle. 1970-1972 - Acting Associate Director, Collaborative R&D Program, National Heart, Lung, and Blood Institute (NHLBI), NIH. 1970-1972 - Associate Director for Lung Programs (NHLBI), NIH. 1971-1972 - Professor of Medicine and Physiology and Biophysics, University of Washington. 1972-1974 - Acting Chief, Pulmonary Branch, NHLBI, NIH. 1972-1980, Director, Division of Lung Diseases, NHLBI, NIH. Present, Associate Director of International Research, NIH, and Director, Fogarty International Center, NIH.

Professional Organizations: Association of American Physicians, American Society for Clinical Investigation, American Physiological Society, American Society for Clinical Research, French Physiological International Federation for Medical Electronics, American Society of Zoologists (Division of Comparative Physiology), Society for Experimental Medicine and Biology, Undersea Medical Society, New York Academy of Sciences.

Honors, Awards: 1956 - Thesis Prize. 1973 - Commendation - Tohoku Medical Society, Sendai, Japan. 1974 - Superior Service Honor Award/DHEW. 1978 - University of California, Los Angeles, Regents' Professor. 1979 - Testimonial Dinner, American Thoracic Society, Las Vegas. 1979 - Honorary Fellow, American College of Chest Physicians. 1980 - Visiting Professor, National Yang-Ming Medical College, Taipei, Taiwan (named Honorary Professor, 1980). 1981 - Honorary Professor - Universidad Peruana Cayetano Heredia, Lima, Peru.

Publications: 170 Scientific Papers.

Editorial Responsibilities: 1970-1976 - American Journal of Physiology and Journal of Applied Physiology--Editorial Board. 1971-1978 - Respiratory Physiology--Editorial Board. 1973-1979 - American Review of Respiratory Disease--Editorial Board. 1973-1975 - Undersea Biomedical Research--Editorial Board. 1975-1984 - Proceedings of Society for Experimental Biology and Medicine--Editorial Board. 1976-1979 - Revue Francaise des Maladies Respiratories--Editorial Board. 1976-1982 - Journal of Applied Physiology: Respiration, Environmental and Exercise Physiology--Associate Editor. 1979-1981 - American Journal of Medicine--Associate Editor. Lung Biology in Health and Disease--24 Volumes Monograph series published by M. Dekker, Inc., New York--Executive Editor (18 volumes published).

QUESTION SUBMITTED BY SENATOR RUDMAN

Support of Gorgas by Other Countries

Officials at the Gorgas Memorial Institute have, in the past, contacted officials in other countries requesting support but to no avail. There have been no recent overtures by Gorgas officials. To the best of our knowledge, neither the Department of Health and Human Services nor the Department of State have approached other Latin American governments with this type of request. Because of the political sensitivities involved in asking one foreign country to provide some support to a laboratory of another, we will contact the State Department and ask them to assist us in pursuing this matter.

Questions Submitted by the Subcommittee

CONFERENCES IN FOREIGN LANDS

Question: What conferences in foreign lands do you intend to fund--and at what cost?

Answer: The Fogarty International Center does not organize conferences to be held in foreign countries. However, a number of grant requests for the support of conferences in foreign lands are received by the Center. These conferences are organized either by American scientists or American professional organizations. On the basis of previous years' experience we anticipate receiving in FY 1983 between 20 and 25 such requests. We estimate that the amount provided in response to these requests will be about $240,000, of which the Fogarty International Center will contribute about $22,000. The balance will be provided by the other NIH institutes and by other agencies.

Question: Are these priority matters--or can they be dispensed with at a time of budget austerity?

Answer: Let me preface my response by saying that we are now supporting fewer conferences than formerly, and that each grant request for conference support competes with other grant applications received by NIH.

We believe that conferences and workshops are an essential means of scientific communication that complements and does not duplicate scientific literature. Conferences provide a forum for debate and for evaluation of ongoing research rather than completed work. The ideas exchanged during a conference represent many viewpoints, and discussions constitute an immediate feedback which often brings about answers to unresolved questions. In addition, conferences provide an opportunity to establish scientist-to-scientist contacts from which long lasting cooperation results.

Again, the annual cost of international conferences is approximately $240,000, representing only a small portion of the total NIH budget. The few conferences that ultimately receive funding are activities of high priority that have survived a rigorous peer review process. Therefore, we believe that the scientific benefits and relatively low cost of these activities warrant their continuation even at a time of budget austerity.

GORGAS MEMORIAL LABORATORY

Question: What major contributions to tropical medicine has the Gorgas Memorial Laboratory made over the past five years?

Answer: While the GML has made numerous contributions over the years to some of the puzzles of tropical disease, we feel that the major contributions it has made within the past five years are the following:

1. Investigating, monitoring, detecting and alerting authorities about spread and epidemic of arboviral diseases--yellow fever, dengue, Venezuelan equine encephalitis and St. Louis encephalitis. Epidemics of asceptic meningitis and acute hemorrhagic conjunctivitis have also been investigated.

2. The design and conduct of environmental impact studies (especially biological and health effects) as applicable to major projects disrupting a tropical jungle setting.

3. Development of a system for testing potential anti-malaria drugs in the owl monkey.

I should also like to point out that the GML has a program concerning the characterization of a specific population group which is at high risk for developing cervical cancer.

Question: Does the World Health Organization play any financing role in the Laboratory's programs?

Answer: The WHO supplements the financing of the GML with grants and contracts, particularly through the Pan American Health Organization, which serves as its regional arm for the Americas. In FY 1981 this amounted to $47,781.

Question: What new progress has been made in the identification of antimalarial drugs?

Answer: During 1981, two new drugs were found to be effective in the treatment of drug-resistant falciparum malaria infections in owl monkeys. While this is only an intermediate step in the process of learning, if these candidate drugs will indeed prove their worth in humans, it is an essential and critical step. These studies are being supported under a contract with the U.S. Army.

LANGUAGE PROVISION

Question: Why do you propose language that eliminates the specific earmark for the Gorgas Memorial Institute?

Answer: The proposed language change does not eliminate the specific earmark for GML; rather, it restores language from previous appropriations which specified that the designated amount for GML could not be exceeded. The Gorgas Memorial Institute would remain as a line item in the Fogarty International Center budget. The proposed language would give the FIC flexibility to distribute budget changes across all activities. This would permit the best programmatic use of appropriated funds.

Question: What budget reductions are you anticipating that would require such a language change?

Answer: During a time of fiscal constraints within the federal government we must be in a position to respond to the wishes of the Administration and the Congress in the most effective and productive way. The suggested language change would enable us to do this.

GORGAS MEMORIAL INSTITUTE FUNDING LEVEL

Question: Is Gorgas a permanent appropriation--or does Congress have some discretion in its funding level?

Answer: The Gorgas Memorial Institute does not have a permanent appropriation, but has a permanent authorization as stated in Public

Law 70-350, May 7, 1928. This law established "...that there is hereby authorized to be permanently appropriated for each year... the sum of not to exceed $50,000 to be paid to the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc...." This law has been amended to gradually increase the total authorization to $2,000,000.

In the annual appropriation process the President may propose and the Congress appropriate any amount not to exceed the $2,000,000 authorization level. In this sense the Gorgas Memorial Institute is no different than any other line item in an appropriation.

INFORMATION DISSEMINATION

Question: Last year you claimed that the United States health sciences community benefits greatly from learning about what is being done in other countries. How specifically do you use this information -- and how do you disseminate this information to the public and to the other Institutes at NIH?

Answer: In most instances significant advances in the health sciences result from the combined accomplishments of a number of investigators not only from different laboratories but from different parts of the world. As I stated in my opening remarks, the United States is no longer the most exclusive site of scientific activities. Many significant results and discoveries are made in other countries. The frequency with which the Nobel Prize is shared by investigators of different nationality is eloquent testimony to the internationality of science.

The benefits of international exchanges are disseminated in three major ways:

(a) We encourage and facilitate collaboration between American scientists and those in other countries. In this way, the new knowledge and techniques developed in foreign countries are brought to the attention of our research scientists in a practical way.

(b) We help to fund the attendance of American scientists at foreign scientific meetings and the attendance of key foreign scientists at scientific meetings held in the USA. This results in productive scientific communications wherein the new knowledge developed abroad is revealed to our scientists in a way that they can question the foreign investigators involved and obtain a full and useful understanding of new data or techniques.

(c) Whenever we provide some financial support for a scientific meeting, held in the USA or abroad, we insist that the scientific proceedings be published so that the information becomes available to our scientists and those in other parts of the world.

The Fogarty International Center uses these three modalities through its Advanced Studies Program and other activities. In all instances, we invite participation by all the NIH Institutes having a mission interest in the subject matter of the study or meeting, as well as other pertinent agencies and organizations.

BUDGET CUTBACKS

Question: If confronted with a major budget cutback, what program elements would Fogarty target for decreased funding and what elements would you like to see maintained at present or increased levels of funding?

Answer: New activities scheduled for initiation in FY 1983 would be eliminated. Conferences of lesser priority would not be funded. We would ask the Gorgas Memorial Institute to share in any reduction, and activities and services related to our bilateral agreements would need to be curtailed. Available resources would be dedicated to the maintenance of the Scholars and Fellowships Programs, and proposed funding increases for higher stipend levels could not be implemented to the extent that they are needed.

It should be noted, however, that the FIC's relatively small budget does not permit a great deal of flexibility in shifting funds from program to program. Even a small cut in the overall FIC budget has a major impact. Major cuts would elminate activities of high priority and might result in reductions in staff.

GENERAL POLICY

Question: Would you outline those major areas of international exchange in the health sciences that have been of greatest benefit to this country?

Answer: I am hesitant to single out only certain areas, as so many benefit us and it is a matter of subjective judgment. I will mention four:

1. Cancer studies - the occurrence of unusual concentrations of types of cancer in certain foreign population groups is of great importance to learning about causative factors.

2. Cardiovascular disease - blood chemical and other studies conducted on an international scale are providing important clues to risk factors for coronary artery disease and hypertension.

3. Infectious diseases - the study of the effectiveness of new and potential vaccines requires the wide and varied geographic settings offered on an international scale.

4. Neurological disorders - much of new knowledge about the slow-virus causation of certain neurologic diseases has resulted from international work.

Question: In terms of biomedical technology transfer, where has the greatest benefit occurred, in your view?

Answer: In terms of biomedical technology transfer, I feel that the greatest benefit is being derived by us from international exchange in the composite area of molecular biology/recombinant DNA/ genetic engineering. This is a large and burgeoning field everywhere. We are learning much from the British, Israelis, Japanese, to name but a few. They are learning much from us as well.

Question: Was the cost of obtaining this benefit commensurate with the benefit?

Answer: Total NIH expenditures in the U.S. and abroad related to international activities currently approximate $60 million a year, about 1.7% of the total FY 82 NIH budget. For example, the proportion of this which goes into the field of molecular biology/recombinant DNA/genetic engineering is very small compared to the domestic expenditure by NIH and industry and as compared to the benefits which we anticipate will be derived in the future from this technology.

NATIONAL LIBRARY OF MEDICINE

STATEMENT OF DR. MARTIN M. CUMMINGS, DIRECTOR

ACCOMPANIED BY:
- KENT A. SMITH, DEPUTY DIRECTOR
- THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
- ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Dr. MALONE. Mr. Chairman, coming to the table are Dr. Martin Cummings, Director of the National Library of Medicine, and Kent Smith, Deputy Director of that library.

Senator RUDMAN. Would you identify again the people at the table because we don't have name tags.

Dr. MALONE. To my left is Dr. Martin M. Cummings, Director of the National Library of Medicine. And to his left is Mr. Kent Smith, the Deputy Director of the National Library of Medicine.

Senator RUDMAN. All right, Dr. Cummings; I know you have testified before the subcommittee for many years, and we welcome you again.

I would like to offer a special welcome to Mr. Smith whose father is an old friend of mine and who, I believe, was also a resident of my home town in New Hampshire.

Mr. SMITH. He still is, sir.

Senator RUDMAN. I believe you were also.

Mr. SMITH. Yes, I was.

Senator RUDMAN. We rarely have people from New Hampshire up here before the committee. Most of them were smart enough to leave which says something about the two of us, Mr. Smith.

Mr. SMITH. Thank you.

OPENING STATEMENT HIGHLIGHTS

Senator RUDMAN. You may proceed.

Dr. CUMMINGS. Mr. Chairman, I am reminded by your kind remarks of another distinguished Senator from New Hampshire who recognized Kent Smith as coming from your State after he heard him speak.

I will attempt in a few minutes, Mr. Chairman, to summarize the work of your National Library of Medicine.

It was founded in 1836 and has since that time been the Nation's major resource for information in biomedical research and education and health-care delivery. In 1956, the Congress recognized the work of the Library and passed the National Library of Medicine Act under whose statute we now continue to provide services to the Nation.

We maintain a collection of about 3 million items. More than half of these represent bound volumes of medical literature. We index a quarter of a million medical articles each year. We catalog about 13,000 medical books each year.

The indices and catalogs are announced monthly so that the scientists and educators of the country know what is available in their National Library. We provide more than 1 million interlibrary loans annually; about a quarter of a million loans are provided directly from the National Library, and three-quarters of a million from a network of regional medical libraries which have been established by the National Library of Medicine.

The main framework of the bibliographic apparatus, the reference services, and the interlibrary loans come from the computer-based system known as MEDLARS. We now have about 1,800 institutions joined together which use the MEDLARS system for access to the medical literature. These represent universities, medical schools, hospitals, particularly community hospitals, Government agencies, and various commercial organizations.

During the last fiscal year, we provided more than 2 million computer searches upon demand. The user pays the full cost of accessing the system.

The newest activity of the National Library of Medicine is to upgrade the MEDLARS system. We believe through this new upgrading that we will make a more efficient contribution to providing medical literature and the information contained within the medical literature to those who need it. We believe we will lower the cost of handling this literature and, therefore, representing a national saving.

We believe that through our centralized cataloging, we will save about $3 million for the Nation which won't have to repeat this cataloging.

Another most significant change will result when we reconfigure our regional medical library network from the present 11 institutions that serve in this capacity down to 7 institutions. We think that this effects cost savings without any inhibition or constraint on the services that they provide.

To continue these activities, we are requesting a budget of $46,043,000 for fiscal year 1983.

I would be pleased to answer any questions or provide material for the record if you desire.

EFFECT OF CONTINUING RESOLUTION

Senator RUDMAN. Thank you, Dr. Cummings. We will have a number of questions for the record.

I would ask you just very quickly if you could give me your answer to the questions I have asked the prior witnesses—essentially, the effect of the continuing resolution at the rate that it is imposed at this time.

Dr. CUMMINGS. The dollar effect of the continuing resolution amounted to about $3.2 million, compared to the President's request. The savings were taken through cutbacks in several programs. The extramural grants were reduced by $1.4 million.

I should point out that this latter decrease was a measure imposed by a reduction in our authorization by the Congress.

In addition, we ourselves reduced our intramural research activities and reduced our intramural audiovisual program activities.

On the management side, we are planning to integrate administratively the National Medical Audiovisual Center with the Lister Hill National Center for Biodmedical Communications. We should have some savings at the top in terms of reducing redundant management costs.

MEDLARS PRICING

Senator RUDMAN. We have some concerns on pricing, if you will, and the cost recovery on these computer systems. And you have had discussions with the committee before on the subject. You went a number of years—I believe 3—without a rate increase. And then last October, online fees went from $8 to $15 for nonprime time and from $15 to $22 for prime time. Did those increases jolt any of your users? Did you have any falloff in the amount of use of your data base?

Dr. CUMMINGS. We have had, I think, the conventional response to the increase in pricing which is a plateauing immediately after the announcement of a new pricing structure, and then the beginning of increased use.

But since we have only had this new pricing in effect for 3½ months, I can't be confident of the significance of the change from the plateau to further increase.

I might say that the greatest reaction to our change in pricing has come not from our on-line hourly charges, but from the change in the method through which we recover costs for leasing our tapes. There has been a very interesting reaction, Mr. Chairman, on the part of one vendor. We have been told that the new prices are too high, and they are somewhat angry with us. And on the part of another commercial vendor, we have been told the pricing is still too low. I feel comfortable that we are somewhere in the middle, and I think that is the most direct answer I can give you.

Senator RUDMAN. When you say in some of the material that you submitted that full costs are recovered, that is certainly of use and access. I don't assume that applies to creation of the data base.

Dr. CUMMINGS. No; that is correct. We do not pass on the cost of acquiring the books and journals nor cataloging them because we believe that is a normal function of the library. But everything that goes beyond that—computer management, computer operations, communication costs, printing, overhead, all of the training that is related to the activity—is passed on to the user.

And I can tell you that we do recover full accessing costs. In fact, Mr. Chairman, we returned about $300,000 to the Treasury last year.

And we expect, since we have just learned that we are recovering about 103 or 106 percent of the cost, depending on whether you use GAO figures or ours, we will probably return more than that amount this year.

Senator RUDMAN. Do you charge the same rates for these services to both commercial, for-profit users and nonprofit users?

Dr. CUMMINGS. Yes, sir, we do.

Senator RUDMAN. And do you think this is reasonable?

Dr. CUMMINGS. Yes; we believe it is reasonable. We believe that the commercial private sector such as the pharmaceutical industry helps support the National Library of Medicine in the same way that physicians and the taxpayers generally do. So all of the charges are identical.

I do know that there are views to the contrary, but I can tell you that the NLM Board of Regents which has examined this issue supports the policy of equal access for equal pricing.

TAPE LICENSING AGREEMENTS

Senator RUDMAN. I want to move onto some of the licensing agreements very briefly. That is a slightly different version of what we are talking about.

It is the committee's understanding you have certain commercial users who essentially have negotiated on-line lease arrangements to your data base and then, of course, are able to extract this and to sell it as a commercial venture to smaller users.

Dr. CUMMINGS. That's right.

Senator RUDMAN. Do you feel that your fee schedule and your lease schedule in terms of what you are receiving is reasonable and fair both in terms of: One, of what it has cost you; and, two, what it may be reaping in profits for them?

Dr. CUMMINGS. Well, let me start in reverse order. We have no way of knowing what profit is being made by the commercial sector which leases our tapes. We can only surmise that they are doing well because in the case of one small business which leased our tapes, it became a large business, sufficiently large to be bought by a conglomerate overseas.

We think it was profitable.

The other company, we also believe is doing reasonably well.

The difficult part of establishing pricing, Mr. Chairman, is to attempt to satisfy the conditions defined in an OMB circular which calls for full cost recovery under certain conditions, the conditions imposed by the Congress, which in the past has been interested in sharing this knowledge with people at all levels so that we don't price the poor and disadvantaged out of access, and the consideration of having domestic and foreign commercial vendors competing for the American market. It is the latter problem that has been the most difficult for us.

The U.S. information industry has grown to be a very important part of society. And I think there is a domestic/foreign competition to gain control of this industry. And we are sort of caught up in that circumstance.

Senator RUDMAN. Of course, you would have some difficulty in assessing how much they are using it because I take it they are leasing it on a flat-rate basis, or is it tied to their subsequent use and sale?

Dr. CUMMINGS. In the past, we had a flat-rate release—$50,000 for the first year, $30,000 each year thereafter. We have changed that structure to a $20,000 minimum subscribing fee, and an hourly use charge with an additional charge for citations that are identified and printed.

This pricing structure has only been in effect a few months. We do not yet know what impact it will have. But we can report back, I think, after 4 or 5 months' experience and answer your question.

CATALOGING BACKLOG

Senator RUDMAN. During the past year, have you had any improvement in your backlog in terms of your cataloging?

Dr. CUMMINGS. Yes; I was hoping someone would ask me that question. It is the most embarrassing question we have had to deal with in recent years.

Senator RUDMAN. Can you give us some empirical data in response to that?

Dr. CUMMINGS. Yes; I am pleased to tell you that the backlog will be reduced by two-thirds, and we are now entering the normal processing arrangement where the backlog equals the capacity of the staff to catalog.

PREPARED STATEMENT AND SUBMITTED QUESTIONS

Senator RUDMAN. Thank you, Dr. Cummings and Mr. Smith, for appearing here today. And we will submit some questions to you for the record. And you will have a chance to correct your transcript testimony at that time.

Thank you very much.

[The statement and the following questions which were not asked at the hearing but were submitted for response for the record follow:]

STATEMENT OF MARTIN M. CUMMINGS

Progress in medicine is dependent on the efficient publication and dissemination of knowledge. Man's brain, remarkable and versatile as it is, simply is not capable of acquiring and retaining the vast amount of new information generated by the biomedical sciences.

The National Library of Medicine is mandated to serve as the nation's principal resource for information needed in biomedical research, health professional education, and the delivery of health care services in both the private and the public sectors. In August 1981, the Library observed the 25th anniversary of this mandate, as embodied in the National Library of Medicine Act of 1956 (P.L. 84-941). Specifically, the Act requires the Library to acquire and preserve the literature of biomedicine, to organize the materials and publish catalogs and indexes, to make this literature available by loan and other methods, and to provide reference services and research assistance. NLM has had remarkable success over the past 25 years in fulfilling these obligations.

This success has been achieved in the face of an enormous, ever-increasing volume of biomedical literature. As an example of the proliferation of scientific literature, James Martin, in his book The Wired Society, estimates that the number of extant scientific journals has increased by tenfold every 50 years since 1750. By 1900 there were 10,000, by 1950, 100,000, and by the year 2000 his projection is an astounding 1,000,000. This increase in volume coupled with rapidly inflating medical publishing costs makes it difficult to keep pace with the knowledge explosion.

In a continuing effort to address this problem, NLM maintains as its highest priority in its FY 1983 budget request the acquisition, organization, and distribution of biomedical literature. The Library has built a collection representing more than 70 languages and containing over 2.5 million items in biomedicine and related fields. To maintain the integrity of this collection, the largest in the world, the Library comprehensively acquires the substantive literature of the health sciences in all its forms, including books, journals, audiovisuals, microforms, and manuscripts. Parallel with the long-term trend of increasing volume of literature is the increased effort required to process, catalog, and index it.

NLM relies heavily upon its online computerized MEDLARS (Medical Literature Analysis and Retrieval System) network to aid in the dissemination of the literature which is acquired and indexed. MEDLINE, the most frequently used of all the 22 constituent data bases contained within MEDLARS, recently marked its tenth anniversary of online services. MEDLINE and all of the other MEDLARS data bases are available in the United States through a network of 1,550 online centers at universities, medical schools, hospitals, government agencies, and commercial organizations. More than two million computer searches of NLM's data bases were performed by these centers in fiscal year 1981. The Library will continue its policy of recovering, through user fees, the full cost of providing online access to its various MEDLARS data bases. In FY 1983, MEDLARS III, NLM's third-generation computer-based system for library and information services, will complete its developmental phase and begin to be implemented. The primary goal of MEDLARS III is to automate more fully many of NLM's basic internal technical processing functions. Labor intensive functions such as cataloging, indexing, circulation, serial check-in and other library functions will become more effective and efficient through automation. MEDLARS III has immense potential for lowering the cost of literature handling and for speeding the delivery of biomedical information to researchers, practitioners, and educators. This project also enjoys top priority in NLM's FY 1983 budget request.

The Regional Medical Library (RML) program, authorized under the Medical Library Assistance Act, is another means through which NLM provides comprehensive medical library services to the nation. Since its initiation in 1967, the RML program has provided for the development and maintenance of a nationwide biomedical information network. The RML system is composed of: (1) the NLM and ten other Regional Medical Libraries that coordinate basic library services to libraries within the regions; (2) over 100 resource libraries (usually academic health science libraries); and (3) approximately 3,000 health science libraries located in hospitals and other health-related institutions.

During 1981 the NLM launched a major effort to evaluate the success of the RML network in providing services, and in attaining optimal level of performance. As a result of the study, the NLM Board of Regents approved a proposed reconfiguration of the RML network at its October 1981 meeting. Beginning in October 1982, the present eleven regions will be reduced to seven. NLM will no longer serve as one of the RML's but will concentrate efforts on developing national programs and providing backup support for document delivery. The new configuration is designed to take advantage of the strong working relationships and programs developed in the regions over the past 14 years. It will provide more effective mechanisms to encourage network cost-sharing, provide a broader base of program support, and reduce dependence on central funding.

The Medical Library Assistance program contains other elements in addition to the RML system. Five different types of grant awards are also funded under this activity to improve national medical library services:

- o Resource Grants assist in the development of adequate health science library collections at the local level, facilitate user access to health information resources, and improve resource sharing among local libraries;
- o Research Grants support activities leading to new knowledge about information access, retrieval, and use, as well as the development and application of new information techniques and methods. A special initiative within this program supports research in the application of computer technology to health information problems;
- o Training Grants promote the integration of computer technology with clinical teaching, practice, and research;
- o Publication Grants provide support for preparing and publishing scientific works of importance to the national health effort which are not commercially profitable.

o Special Scientific Project Grants provide support for scientists, practitioners, and scholars to prepare book length interpretive analyses of the existing literature on important major health problems or topics.

As an example of the achievements realized through current NLM grant support, I would like to describe one particular project. Dr. Howard Bleich, of Beth Israel Hospital in Boston, has developed a computer program based on MEDLINE citations that provides an inexpensive and efficient means of searching for literature known to be held locally and thus immediately available. This system, known as "Paper Chase," is quick and easy for the hospital staff to use when more exhaustive searches of MEDLINE's 3,000 journals are not required. The achievements of this system, and the national interest generated following a recent article in the New England Journal of Medicine, have resulted in utilization of the system at other hospital locations.

Progress in biomedical research depends on the dissemination of research results, and in turn, improvement in dissemination of research results depends on innovative research on the application of new technology for improved information handling. The Lister Hill National Center for Biomedical Communications (LHC) is the research and development component of NLM created by Congress in 1968. A team of information and computer scientists and health professionals of various specialties is exploring more effective uses of information processing technology to support the medical community.

During their recent review of the Lister Hill Center's research program, the NLM Board of Scientific Counselors recommended that a high priority be assigned to the Knowledge Base research program. This pioneering effort is developing "knowledge based" systems which will give online access to new medical findings and to practicing physicians. Knowledge bases are founded on biomedical literature that is carefully reviewed, condensed, synthesized, and regularly updated. Such a system, if operational, would be a significant alternative to NLM's traditional methods of collecting literature as published and providing bibliographic access to this information. Viral hepatitis, peptic ulcer, and human genetics are the subjects under study in the Knowledge Base research program.

This year, the activities and functions of the National Medical Audiovisual Center (NMAC), will be integrated with those in the Lister Hill Center. The primary mission of NMAC is to improve the transfer of health science information from research into practice through the creative and effective use of audiovisual materials and technologies. Activities of NMAC are natural complements of those conducted by the Lister Hill National Center for Biomedical Communications. The integration of these two programs will result in more efficient performance through the sharing of administrative and technical resources.

An issue of much concern to the biomedical community is prevention research. While the National Library of Medicine does not actually perform research on disease prevention, it does provide information support for prevention as well as other biomedical activities by serving as the nation's principal resource for biomedical information. One of NLM's most important prevention-related activities is the Toxicology Information Program. This activity provides specialized information services in toxicology and environmental health by creating online data bases such as TOXLINE and CHEMLINE. This program also provides specialized services through an interagency agreement with the Oak Ridge National Laboratory, and supports interagency activities such as the National Toxicology Program (NTP).

Mr. Chairman, our request of $46,043,000 for FY 1983 represents an increase of $1,641,000 over FY 1982. I shall be pleased to answer questions and supply any additional information desired for the record.

BIOGRAPHICAL SKETCH

NAME:
Martin Marc Cummings

POSITION:
Director, National Library of Medicine

BIRTHPLACE AND DATE:
Camden, New Jersey, September 7, 1920

EDUCATION:
B.S., Bucknell University, 1941
M.D., Duke University, 1944

HONORARY DEGREES:
Honorary Doctor of Science, Bucknell University, 1969
Honorary Doctor of Science, University of Nebraska, 1971
Honorary Doctor of Science, Emory University, 1971
Honorary Doctor of Humane Letters, Georgetown University, 1971
Honorary Doctor of Medicine, Karolinska Institute, Stockholm, Sweden, 1972
Doctor Honoris Causa, Academy of Medicine, Lodz, Poland, 1977

EXPERIENCE:
1964 to Present: Director, National Library of Medicine
1963-1964: Associate Director for Research Grants, National Institutes of Health
1961-1963: Chief, Office of International Research, National Institutes of Health
1959-1961: Professor of Microbiology and Chairman, Department of Microbiology, University of Oklahoma School of Medicine
1953-1959: Director, Research Services, Veterans Administration Central Office
1953-1959: Special Lecturer in Microbiology, George Washington University School of Medicine
1953: Associate Professor of Bacteriology, Emory University
1949-1953: Chief, Tuberculosis Research Laboratory, Veterans Administration Hospital of Atlanta
1948-1953: Instructor through Associate Professor of Medicine, Emory University
1947-1949: Director, Tuberculosis Evaluation Laboratory, Communicable Disease Center, U.S. Public Health Service
1945-1947: Assistant Resident Medicine, Boston Marine Hospital
1944-1945: Intern, Boston Marine Hospital
1942-1944: U.S. Army (ASTP)

PROFESSIONAL ASSOCIATION:
American Academy of Microbiology, Inc.
American Association for the Advancement of Science, Board of Directors
American Board of Microbiology
American Clinical and Climatological Association
American Federation for Clinical Research (Emeritus)

American Osler Society, President
American Society for Clinical Investigation (Emeritus)
Association of Research Libraries
Gorgas Memorial Foundation, Board of Directors
Institute of Medicine, National Academy of Sciences
Medical Library Association
Society of Sigma Xi
Washington Society for the History of Medicine

SPECIAL AWARDS AND HONORS:

Veterans Administration Exceptional Service Medal
DHEW Superior Service Award
DHEW Distinguished Service Award
Distinguished Alumnus Award, Duke University, 1969
Honorary Member, Alpha Omega Alpha
Honorary Fellowship, College of Physicians, Philadelphia, 1973
Rockefeller Public Service Award, 1973
Honorary Member, American Medical Writers Association, 1974
Alumnus Membership, Phi Beta Kappa, 1974
Modern Medicine Distinguished Achievement Award, 1976
Distinguished Service Award and Honorary Fellowship, College of Cardiology, 1978
Honorary Member, Academy of Medicine of the Institute of Chile, 1978
Certificate of appreciation for outstanding contributions to medical communication and to the American Medical Writers Association, 1978
John C. Leonard Award, Association for Hospital Medical Education, 1979
Harold Swanberg Distinguished Service Award, American Medical Writers Association, 1979
Fellow, American Association for the Advancement of Science, 1980
105 scientific and historical publications, co-author of textbooks in the field of tuberculosis

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

NLM DATABASE FEES

Question: Why were the online fees charged to foreign users not increased until January 1982 while the increase was effective for domestic users on October 1, 1981?

Answer: Normally fees for domestic and foreign online users are implemented at the same time. Although the fee schedules for both are now $22/15 in prime and non-prime time, it should be emphasized that a foreign center pays both the domestic communication costs (contained in the hourly fee) as well as all international communication costs. The net effect is that foreign centers online to NLM pay approximately $6.00 more a connect hour than a comparable domestic user.

The NLM Board of Regents determines the pricing policy for user fees. Because the Board reviewed domestic pricing policy at a different meeting than foreign pricing policy, the increases in these respective user charges were implemented at different dates.

Question: To what extent is the NLM rate structure competitive with fees charged by private-for-profit groups providing similar services?

Answer: NLM leases its databases to information vendors at prices that evidently allow such firms to make a profit while remaining price competitive with NLM. One vendor, since its founding, has maintained a price structure almost identical to NLM's.

Question: How much revenue does the NLM system generate annually?

Answer: It is estimated that in FY 1982 approximately $4.5 million will be collected for user fees.

Question: Is the revenue sufficient to cover the full costs of your system?

Answer: The full cost of providing access to the NLM online system is being recovered through the collection of user fees. We do not recover costs for acquiring books and journals nor for indexing and cataloging them since these are essential library functions.

LEASING OF NLM DATABASES

Question: What protections have you built into the billing and collections process to insure that commercial vendors accurately reimburse you for NLM services?

Answer: NLM enters into agreements with commercial vendors to lease our databases. Under new licensing agreements, a vendor is required to submit monthly reports to NLM outlining the connect hours and citations printed offline for that period. The license also stipulates usage reports are subject to an audit by the NLM.

Question: Are there, or should there be any limits on the extent to which foreign countries may retail information they buy from the Library?

Answer: NLM's international bilateral agreements are not with commercial vendors but with an institution designated by another country to serve as a national biomedical information resource. The other countries' policies determine the pricing structure for these centers' services. NLM's international agreements do not permit replication of its tapes or the duplication of existing NLM/GPO products. Foreign MEDLARS centers may not provide online services to those countries specified by the Office of Export Administration, Department of Commerce, without prior approval from Commerce.

MEDLARS III

Question: MEDLARS III is a new bibliographic information retrieval system. It will, among other things, allow the user to enter a single search to be run against multiple files using common English commands rather than artificial computer language. What is, or will be, the full cost of this system?

Answer: The FY 1982 budget commitment for MEDLARS III is $1.5 million dollars. The budget request for FY 1983 is $2.3 million dollars. In March the Library will be issuing a Request for Proposal for design and implementation of the MEDLARS III system. Any further details on the estimated costs could introduce a bias in the competitive procurement.

Question: What is your statutory authority for undertaking this project?

Answer: The statutory authority for projects such as MEDLARS III is in the Public Health Service Act (42 U.S.C. 275), Title III, Part I, Section 382, a part of the basic legislative authority of NLM.

Question: Has there ever been an independent evaluation of MEDLARS, and if not, why not?

Answer: The MEDLARS system has received extensive and independent evaluation since it was implemented in 1964. A landmark study by Professor Wilf Lancaster initiated in 1966 was an important factor in defining the requirements for MEDLARS II. Since that time a number of evaluation studies have been published ranging from individual assessments by health practitioners and information specialists to detailed comparative evaluations of MEDLARS and other similar data base systems. A partial list of recent studies derived from our MEDLARS system follows. A recent study under the auspices of the Office of Technology Assessment will be completed this year.

MEDLARS Evaluation Studies
(A selected list 1966-1982)

1966

Hogan R. An evaluation of MEDLARS output: Demand and recurring bibliographies. Bull. Med. Libr. Assoc. 1966 Oct; 54: 3[illegible]1-8.

1968

Lancaster FW. Evaluation of the MEDLARS demand search service. Bethesda, Maryland: National Library of Medicine, 1968.

1969

Lancaster FW. MEDLARS: Report on the evaluation of its operating efficiency. Amer. Documentation 1969; 20:119-42.

Salton GA. A comparison between manual and automatic indexing methods. Amer. Documentation 1969 Jan; 20:61-71.

1970

Goode DJ, Penry JK, and Caponio JF. Comparative analysis of Epilepsy Abstracts and a MEDLARS bibliography. Bull. Med. Libr. Assoc. 1970 Jan; 58;44-50.

1971

Lancaster FW. Evaluation of on-line searching in MEDLARS (AIM-TWX) by biomedical practitioners. A report to the National Library of Medicine. Urbana, Ill. University of Illinois Graduate School of Library Science, 1971.

1972

Salton GA. A new comparison between conventional indexing (MEDLARS) and automatic text processing (SMART). J. Am. Soc. Inf. Sci. 1972 Mar-Apr; 23:75-84.

1974
McCarthy SE, Maccabee SS, and Feng CCH. Evaluation of MEDLINE service by user survey. Bull. Med. Libr. Assoc. 1974 Oct; 62:367-73.

Moll W. MEDLINE evaluation study. Bull. Med. Libr. Assoc. 1974 Apr; 62:1-5.

1976
Hubber AL, Moll W. A broken hip and MEDLINE: A case report. Bull. Med. Libr. Assoc. 1976 Jul; 64:320-22.

Sewell W, Bevan A. Nonmediated use of MEDLINE and TOXLINE by pathologists and pharmacists. Bull. Med. Libr. Assoc. 1976 Oct; 64:382-91.

1977
Brodauf H, Hoffman WD, Klawiter-Pommer JH. Searching the literature of veterinary science: a comparative study of the use of 10 information systems for retrospective searches from January 1972 to December 1974. Vet. Rec. 1977 Dec.3; 101:461-3.

Tagliacozzo R. Estimating the satisfaction of information users. Bull. Med. Libr. Assoc. 1977 Apr; 65:243-9.

1979
Burrows S, Kyle S. Searching the MEDLARS file on NLM and BRS a comparative study. Bull. Med. Libr. Assoc. 1979 Jan; 67:15-24.

Cluxton RJ Jr, Hunter RH, and Reed RC. Comparison of five information services as sources for bioavail ability data. Am.J. Hosp. Pharm. 1979 Sep; 36:1215-8.

1980
McGee JL. A MEDLINE feasibility study. Bull. Med. Libr. Assoc. 1980 Jul; 68:278-87.

Pinhas N. Data-banks: a comparative study of INSERM AND NLM data-banks. Med. Inf. (Lond) 1980 Jan-Mar; 5:85-97.

1982
Carson S, Wyatt HV. Retrieving reference on microbiology: which secondary publications can help? ASM News 1982 Jan; 48:5-9.

NLM CATALOGING BACKLOG

Question: What are your plans for fiscal 1983 to reduce the backlog?

Answer: According to current projections, there will be about 5,000-6,000 books remaining in the cataloging backlog at the beginning of fiscal 1983. These constitute a normal working backlog.

Question: I believe you stated in 1980 that the Library had a backlog of at least 15,000 books that had never been cataloged. It was also estimated at that time that the backlog would grow to over 25,000 volumes by 1981. Where do matters presently stand?

Answer: The growth of the backlog was stopped during 1981, and the backlog has now been reduced to below the 1980 level. The backlog included 19,410 books on May 1, 1981. Some 6,689 items were removed between May 1, 1981, and January 31, 1982.

Question: What is the current level of that backlog?

Answer: As of January 31, 1982, there were 12,721 books remaining in the backlog.

Question: To what extent have any of the manpower shortages in dealing with the backlog been remedied?

Answer: Two of five long standing cataloger vacancies were filled in November 1981. The two new employees are completing their training period. Approval to hire two additional experienced catalogers from outside the Department was granted on February 25, 1982. These two people will begin work in March. One cataloger vacancy remains.

Question: Didn't you tell us you intend to deal with some of the backlog problems by reallocating the present staff in various ways?

Answer: During the past year, several library staff members from outside the cataloging area were detailed part-time to assist with cataloging backlogged items. This reallocation contributed significantly to the reduction in the backlog achieved to date. It cannot continue indefinitely without adverse impact on other important library functions.

REGIONAL LIBRARIES

Question: Please explain why you plan to reduce the number of regions involved in the Regional Medical Library Network from 11 to 7?

Answer: The experience NLM has had since the inception of the program indicates that larger geographical areas can be administered effectively. NLM believes that by building on the network already developed and utilizing improved communications the program can adapt to anticipated current and future budget constraints through a reconfiguration of the existing regions. The aim is to provide more cost effective regional groupings while preserving or improving the present level of service to health professionals. Funding for overhead and administrative functions will be reduced and the dollars saved will be funneled to direct program support.

Question: What regions will be absorbed and what reaction have you had from areas involved?

Answer: The reconfiguration was accomplished by merging the three existing regions in the northeast into one region; the two regions in the midwest into one region; and the Mid-Atlantic Region and the Southeast Region into one region. The Midcontinental, Northwestern, Southwestern and Southcentral Regions remain unchanged.

Reaction to configuration has been generally positive, and we anticipate strong candidates for the RML in all of the regions, including those that have been reconfigured.

ADMINISTRATIVE SAVINGS

Question: In light of current constraints on the budget, and the need to put adequate funds into research, what savings can you achieve in direct operations and program management in Fiscal 1983?

Answer: The FY 1983 request for these two administrative activities has been held to an absolute minimum. The budget request provides only for such mandatory increases as within-grade pay increases, Federal Telecommunications System rate increase, increased surcharges for the NIH service and supply fund procurement system, and pay raise costs. In Intramural Research, specific administrative savings will result from the integration of the Lister Hill Center and the National Medical Audiovisual Center. We also expect administrative savings to result from the implementation of MEDLARS III.

Question: What are your most important administrative concerns--and what are your least important concerns?

Answer: The most important concern is to provide higher quality services to the nation in a cost effective manner. The Direct Operations activity provides administrative management and scientific direction of NLM's grant and Regional Medical Library (RML) contract programs authorized by the Medical Library Assistance Act (MLAA). Program Management provides the overall planning, administration, coordination, evaluation, and direction of the NLM programs. Each of these functions is critical for the fulfillment of NLM's mission.

Question: What criteria do you use for determining your administrative priorities?

Answer: It is the policy of NLM to allocate the minimum amount of resources required to perform its essential administrative functions. The policies are determined by senior management staff. The highest priority is given to administrative support of library services and products.

MEDICAL LIBRARY ASSISTANCE PROGRAM

Question: Last year the appropriation for the Medical Library Assistance Program was reduced to $7.5 million to align it with the new authorization level. What has been the effect of this reduction of some $2.3 million over the 1981 operating level?

Answer: The immediate impact of the $7.5 million budget level, representing a 24% reduction from the FY 1981 level and a 16% reduction from the President's FY 1982 budget request, has been a cut in the number of new awards by almost half (from 66 to 36), as well as reducing support levels for continuation awards to projects in progress. The larger, overall effect on the Medical Library Assistance Program has been to slow nation-wide progress in improving health information access, and to inject a degree of instability in the research activities of computer scientists, librarians and health information specialists, and others seeking to discover and implement better ways of utilizing health knowledge.

BENEFITS FROM MEDLARS III

Question: NLM has an excellent record of utilizing modern technology to improve the dissemination of medical information. What improved services will result from your latest MEDLARS III developmental efforts?

Answer: MEDLARS III is NLM's third-generation computer-based system for library and information services. The primary goal of MEDLARS III is to more fully automate many of NLM's basic internal technical processing functions. Labor intensive functions such as cataloging, indexing, circulation, serial check-in, and other library functions will become more effective and efficient through automation. MEDLARS III will not only provide improved services but will provide cost benefits over its life that will greatly exceed the development costs.

MEDLINE AND MEDLARS

Question: What is the relationship of the MEDLARS retrieval system to MEDLINE? Will one replace--or augment--the other?

Answer: The term MEDLARS is an acronym for Medical Literature Analysis and Retrieval System. This computerized system has two principle products: a series of bibliographic publications of which the monthly Index Medicus is best known, and a series of data bases accessible online from computer terminals around the world, of which MEDLINE is the largest and most frequently used. A new updated version of MEDLARS, called MEDLARS III, is presently under development. It will contain all of the elements described above, including MEDLINE, and will automate such internal library functions as ordering, receiving, and cataloging materials.

Question: You are reducing several other activities, including the Lister Hill Center, in order to pay for retrieval services. Why is this?

Answer: The NLM's FY 1983 budget request includes reductions for the Lister Hill Center, the National Medical Audiovisual Center, and the Toxicology Information Program. These decreases were necessary in order to maintain quality basic library services to the biomedical community. Provision of these services remains our highest priority. Access to online retrieval services is paid for by the users.

Question: Does this suggest that your user fees may not be high enough?

Answer: NLM charges the full cost to access its system, a charge that provides equal access to all users. This is the policy recommended by the NLM Board of Regents also. This policy of charging full accessing costs is consistent with a recommendation contained in the National Commission on Library and Information Science's recent report on public sector/private sector interaction in providing information services.

RESEARCH PROGRAMS

Question: Wasn't it your intention, in the event of budget cuts, to protect direct services to the health professional community and sacrifice some elements of their R&D programs? What has happened?

Answer: Both the FY 1982 continuing resolution and the FY 1983 budget request do protect the Library Operations activity, which provides essential national library services to the biomedical community. Reductions were taken in NLM's other intramural programs, including research and development activities.

Question: How much of your total budget is spent on extramural and intramural research and development programs?

Answer: $7,460,000 of the total NLM budget will be spent on research and development programs in FY 1983.

Question: How much could be cut from these programs and still leave the basic functions intact?

Answer: NLM's research and development budget request for FY 1983 is below that of FY 1981. This level of support is at an absolute minimum. Any additional decreases would reduce these activities below critical mass and destroy the momentum of the program.

OTA REPORT

Question: Please comment on the observation by the Office of Technology Assessment that a possible "Weak Link" in NLM's information dissemination efforts "may not be the technology of MEDLARS, but the characteristics of its users." What steps are you taking to alleviate this problem?

Answer: We believe OTA's observation refers to the experience or training of online searchers. Inexperienced or untrained searchers may not be able to use the full capability of MEDLARS technology, hence could produce incomplete or unsatisfactory searches. NLM offers a variety of training courses for searchers, using approaches and material suitable for novices, as well as for partially experienced information specialists and reference librarians. Training is offered at the Library itself in Bethesda as well as at sites in the midwest and west coast. Training ranges from a one-week intensive basic course to 2-3 day specialized courses for advanced candidates and for "back-up" searchers. The National Library of Medicine offers a more comprehensive program of basic training and continuing education for searchers of NLM data bases than any other provider of data base services.

LISTER HILL CENTER

Question: The Lister Hill National Center for Biomedical Communications is the research and development arm of the Library. A principal effort of the Center is to develop "knowledge-based systems" which would provide up-to-date, authoritative answers to questions pertaining to patient care and health care delivery. In your Knowledge Base Program, for what topics are you currently developing information systems?

Answer: The Knowledge Base Research Program is principally a research effort which experiments with methods for the computer acquisition, representation and modification of knowledge structures, to be complemented by user-friendly access. Textual and visual materials, with associated references, are the substantive content being utilized in the medical computer science research efforts exploring coordinated knowledge structures, representations and retrieval strategies to aid in diagnosis, prognosis and treatment of disorders. The three medical areas currently being studied are human genetics (which covers more than several thousand disorders), viral hepatitis and peptic ulcer.

Question: When will these systems be ready for application to patient care?

Answer: We hope that prototype knowledge-based systems should be available to allow evaluative feasibility testing by selected members of the potential user community within three years.

ADMINISTRATION

STATEMENT OF CALVIN B. BALDWIN, ASSOCIATE DIRECTOR FOR ADMINISTRATION

ACCOMPANIED BY:
EDWIN D. BECKER, ASSOCIATE DIRECTOR FOR RESEARCH SERVICES
THOMAS E. MALONE, ACTING DIRECTOR, NATIONAL INSTITUTES OF HEALTH
ANTHONY ITTEILAG, DEPUTY ASSISTANT SECRETARY, BUDGET, DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCOMMITTEE PROCEDURE

Senator RUDMAN. The next witness is going to be Calvin Baldwin, Associate Director for Administration of NIH. Mr. Baldwin is here to testify about the funding needs of the Office of the Director of NIH and the buildings and facilities program.

Mr. Baldwin, welcome. We would appreciate it very much if you would provide us with a brief summary, and your entire statement will be included in the record.

INTRODUCTION OF ASSOCIATES

Mr. BALDWIN. Thank you, Mr. Chairman.

I would like to introduce on my left Dr. Edwin Becker who is the Associate Director for Research Services. Dr. Becker's responsibilities include the areas of safety, administrative services, and our construction and our engineering efforts.

My testimony covers two appropriations: First, the appropriation for the Office of the Director, which includes the Director and the staff to assist him in the administration and coordination of NIH programs, and for administrative support functions such as budget, accounting and personnel. The 1983 appropriation request for the Office of the Director is $24,283,000, an increase of $1,721,000 over the 1982 level. This request will maintain the Office of the Director at its current level.

The second appropriation for which I am testifying is buildings and facilities. This appropriation request for $17,500,000 provides funds for design, construction, and repair and improvement of NIH's facilities. Many of NIH's buildings are in need of rehabilitation and modernization, partly to correct serious fire and safety hazards.

We are requesting $6,600,000 to continue the modernization of our clinical center, the building that houses all of the patient care and clinical research programs at NIH.

16-040 O - 83 - 44

We are also requesting $5 million to begin the long-term rehabilitation of six of our 40-year-old laboratory buildings.

That is a brief summary, Mr. Chairman. I would be glad to answer questions, as would Dr. Becker.

EFFECT OF CONTINUING RESOLUTION

Senator RUDMAN. Just for the record here today, tell us the effect of the continuing resolution, your frank appraisal on your part of the operation.

Mr. BALDWIN. We are maintaining the Office of the Director at approximately its current level.

I might say, Mr. Chairman, that I have spent almost 29 years at NIH now, and I have never seen a greater sense of cost consciousness at the NIH.

Of necessity, in my particular area, we are giving a great deal of emphasis to doing more things on the computer. For example, we are computerizing our procurement activities, and we are paying our bills on time and, as a result, are getting discounts because we have been able to run those operations more efficiently. I might add that the OMB has under consideration a request for supplemental funds for the Office of the Director for the October 1981 pay raise.

Senator RUDMAN. If per chance, you are required to operate at a funding level below the request level or even, say, fiscal 1982 level, would you be able to achieve any additional savings in administrative costs?

Mr. BALDWIN. I believe, sir, if we had to go below the current level, we probably would have to do something more drastic such as lowering the employment level as I see other agencies doing. We have not had to resort to that yet.

PASSENGER VEHICLES

Senator RUDMAN. Let me just refer to one item that seems very minor in the billions that we are talking about, but again these components all tend to be small. You are again requesting authority for 13 passenger vehicles. I am curious to ask how much that will cost, and are they absolutely necessary to be replaced this year?

Mr. BALDWIN. May I ask Dr. Becker to answer that question?

Dr. BECKER. I can't give you the answer, Mr. Chairman, in terms of the amount, but will submit that for the record. I can tell you that as a result of a shortage of funds last year, we did not replace any vehicles except for one police car and an ambulance. There is a time at which it is most economical to replace rather than to continue to use those vehicles and incur substantial repair costs.

[The information follows:]

PASSENGER VEHICLES

In fiscal year 1983, we anticipate replacing seven cars with subcompact cars that are more energy efficient, and several station wagons. The current price limitation is $6,000 for passenger sedans and $6,400 for station wagons, exclusive of additional options, for example power steering and special reinforcement for police vehicles. The vehicles are used largely for transportation of staff and deliveries of mail between the NIH campus and our four major rented office buildings in Bethesda, the Gerontology Research Center in Baltimore, and the Frederick Cancer Research Center.

Senator RUDMAN. Are these very old vehicles?

Dr. BECKER. The vehicles vary in terms of their age. And I will have to submit for the record any details on the miles and the ages of the vehicles.

[The information follows:]

AGE OF PASSENGER VEHICLES

GSA replacement standards (FPMR 101-38.9) state that passenger vehicles may be replaced after being operated for 6 years or 60,000 miles, whichever comes first. On the average, NIH replaces vehicles that are between 8 and 10 years old with mileage over 75,000 miles. Additionally, our motor pool area adheres to a strict maintenance schedule. Each vehicle has a maintenance cost record, and, when it becomes apparent that it is no longer cost beneficial to provide continued maintenance on the vehicle, it is scheduled for replacement. The cars scheduled for replacement in fiscal year 1983 have mileage of 70,000 to 90,000 or are beyond repair.

Mr. BALDWIN. I believe, Mr. Chairman, we are doing that on a schedule that is provided by GSA.

Senator RUDMAN. Right.

I guess the basic point here that we might choose to make is that if you didn't get them again this year, I expect you would still be able to get over here for the hearings all right.

Mr. BALDWIN. I expect that's correct.

REHABILITATION OF LABORATORY BUILDINGS

Senator RUDMAN. In terms of budget austerity, is it possible that you could defer without any serious effects the rehabilitation of some of these laboratory buildings which are structurally sound, but are obviously in need of some upgrading? Could that be deferred another year?

Dr. BECKER. May I answer that, Mr. Chairman?

Senator RUDMAN. You may.

Dr. BECKER. These buildings have been operational for about 40 years.

Senator RUDMAN. How long?

Dr. BECKER. About 40 years. There is no reason why they can't be used for another 40 years in terms of their structure. The problem is the various support systems—the ventilation, plumbing, and to some extent the electrical systems. We have been trying to maintain the buildings as well as possible, and I can say that personally, I have been doing research in one of them for the last 25 years and am familiar in detail with many of the problems.

For example, it is not possible for us to provide the sort of ventilation and air supply to the hoods that we need for safe experimentation. The use of the buildings has changed over a period of years. Some of the buildings are used heavily for chemistry now, in some cases dealing with carcinogenic materials.

We find that only 15 of the 179 hoods meet the standards of the Occupational Safety and Health Administration. We can't improve that unless we can provide more air to the building. And that involves a major change in the entire system.

It is inconceivable that the buildings can be upgraded to the extent they should be while occupied. Therefore, we have developed a long-term plan—it will take about 12 years to complete—whereby we will improve one building at a time. We have been thinking about this and making plans for it for a number of years and have concluded that we should start on this 12-year effort.

CLINICAL CENTER MODERNIZATION

Senator RUDMAN. How is the 9-year program coming along for the clinical center which was started in 1979?

Dr. BECKER. It is moving along very well. We have many projects which can be done sequentially.

In terms of your request earlier about the reduction and the continuing resolution, we lost about $400,000 which means that some small projects have had to be deferred. It has not been a substantial problem, but we are continuing with the improvement in the patient-care areas and many other aspects of the clinical center.

Senator RUDMAN. Is there any disruption out there in terms of patient care, other activities, because of this program?

Dr. BECKER. Well, there is always some disruption.

Senator RUDMAN. I am talking about major disruption.

Dr. BECKER. It has all been phased. We move patients, for example, from one area to another so we can close one patient-care area while we renovate that and use other patient-care areas. We normally have about two patient-care areas closed at any one time.

PREPARED STATEMENT AND SUBMITTED QUESTIONS

Senator RUDMAN. We have some additional questions which we will submit for the record. And then when you are returning your transcript, you will please answer them at that time.

[The statement and the following questions which were not asked at the hearing but were submitted for response for the record follow:]

STATEMENT OF CALVIN B. BALDWIN

I am pleased to have the opportunity to discuss with the Committee the Office of the Director of the National Institutes of Health and the Buildings and Facilities fund of the NIH.

Office of the Director

For reasons of efficiency and economy in operations, funds for the overall direction and administration of the National Institutes of Health and for the centralized provision of a number of very essential support services are provided on a consolidated basis through the appropriation to the Office of the Director.

The appropriation is divided into two budget activities -- Program Management and Direct Operations.

The Program Management activity funds those components of the central administration which are primarily responsible for the development of NIH-wide policy and procedures and the coordination of program activities. Chief among these offices is the Immediate Office of the Director, including the principal associates of the Director and staff officers who provide advice and assistance in the administration and coordination of the intramural and extramural research programs of the Bureaus, Institutes and Divisions.

Other offices supported by the Program Management portion of the appropriation provide leadership in such areas as equal opportunity, program planning and evaluation, disease prevention, medical applications of research, public and scientific communication, protection from research risks, management analysis and review, contracts and grant administration and budget and personnel management. Through these offices are implemented the congressionally mandated programs, Executive Branch priorities, and various initiatives, which the Director deems necessary in carrying out the agency's prescribed mission. These offices are assisted in their efforts by numerous formal and informal advisory groups, both internal and external to the NIH, representing a wide array of viewpoints on issues central to the administration of biomedical research.

The Direct Operations activity of this appropriation provides for the administration and operation of NIH accounting functions and certain personnel activities. The accounting functions supported include financial analysis and reporting, auditing and processing of vouchers, payment of invoices, and the settlement of claims. Personnel services include counseling, training, and a wide range of similar services for over 11,000 employees.

Appropriation Request: Mr. Chairman, the appropriation request for 1983 for the Office of the Director is $24,283,000, an increase of $1,721,000 over the 1982 level of $22,562,000. The requested increase is comprised of mandatory items. This budget request will provide the resources necessary to maintain the Office of the Director at the current level of effort.

Buildings and Facilities

The second appropriation for which I am testifying is the Buildings and Facilities appropriation which provides funds for the design, construction, and repair and improvement of buildings and supporting facilities for the National Institutes of Health.

The appropriation request of $17,500,000 in fiscal year 1983 is for the following:

Rehabilitation of Laboratory Buildings 2, 3, 4, 5, 7 and 8: We are requesting $5,000,000 in FY 1983 to provide for the first building to be renovated as part of a long-term rehabilitation effort. These laboratory buildings have been operational for approximately 40 years, and while they are structurally sound, the support systems and interior architectural features are inadequate in capacity and/or are badly deteriorated. Also, the renovated buildings will meet the requirements of the handicapped, new life safety code requirements and energy conservation provisions.

The 1983 request represents the first phase in the expansion/renovation of Building 8. The total Building 8 project is estimated to cost $11,800,000 in 1983 dollars. Design funds were furnished in FY 1981 and design has been initiated. Funds were also included in the 1981 Appropriation for refurbishing space in order to relocate the programs in Building 8, and that process is underway.

Clinical Center Modernization: The Clinical Center, a 29-year old building, houses all the patient care and clinical research programs of the National Institutes of Health at Bethesda, as well as some of the basic research programs. In FY 1983, we are requesting $6,600,000 to continue the modernization of this building which began in 1979 and is required in order to meet with modern fire and safety codes and to improve functional and environmental components. The program, involving more than 50 projects, is scheduled over 10 years so that clinical and basic research can remain operational during the entire modernization period.

Repairs and Improvements - Plant: We are requesting $1,620,000 to continue the program of major repairs and improvements to the various electrical, mechanical and structural components of the physical plants at Bethesda, Poolesville, and Baltimore, Maryland; Hamilton, Montana; Research Triangle Park, North Carolina; and other field stations for which NIH is responsible. The physical plants are quite extensive and many of the buildings and supporting facilities have been in service for four decades. There is a recurring need to provide for the repair and upgrading of physical plants.

Repairs and Improvements - Program: A funding level of $2,580,000 is also requested to continue the financing of alterations directly related to program needs. The work includes changes in physical facilities to accommodate revisions and new initiatives in research efforts.

Expansion of Radioactive/Hazardous Waste Areas, Building 21: $1,000,000 is requested in FY 1983 for expansion of Building 21 to safely handle low level (medical level) radioactive waste in compliance with applicable regulations. Provisions must be made for volume reduction of radioactive waste through increased segregation, compaction, decay storage, and other volume reduction techniques. Existing facilities are seriously overburdened and space for new activities is not available.

Energy Conservation: A funding level of $700,000 is requested in FY 1983 to provide for installation of sun screens on the east and south facade of Building 31C and double-glazing of windows on the north side of the building. The installation of the sun screens on Buildings 31A and B has been found to be beneficial in reducing the cooling load and in saving energy.

Thank you. I shall be happy to respond to any questions you may have.

Biographical Sketch

NAME : Calvin B. Baldwin, Jr.

BIRTHPLACE AND DATE: Radford, Virginia; December 22, 1925

PRESENT POSITION AND TITLE : Associate Director for Administration, NIH

EDUCATION
- June 1943 : Bethesda-Chevy Chase High School, Bethesda, Md.
- June 1949 : University of North Carolina, Chapel Hill, N.C.--A.B.
- 1949-1951 : University of North Carolina, Chapel Hill, N.C.
- 1952-1953 : American University, Washington, D.C.
- 1960-1961 : Harvard University, Cambridge, Mass.--M.P.A.

EXPERIENCE
- 1980-Present : Associate Director for Administration, NIH
- 1970-1980 : Executive Officer, National Cancer Institute, NIH
- 1963-1970 : Executive Officer, National Institute of Child Health and Human Development, NIH
- 1962-1963 : Assistant Chief, Grants Management Branch, Division of Research Grants, NIH
- 1961-1962 : Executive Officer, Division of General Medical Sciences, NIH
- 1958-1961 : Administrative Officer, Division of General Medical Sciences, NIH
- 1957-1958 : Administrative Officer, Division of Research Services, NIH
- 1955-1957 : Budget Examiner, Office of the Director, National Institutes of Health
- 1953-1955 : Organization and Methods Examiner, National Institutes of Health, PHS, DHEW, Bethesda, Md.
- 9/52-2/53 : Civil Service Intern, Federal Security Agency, PHS
- 1951-1953 : Methods Examiner, Federal Security Agency, Public Health Service, Washington, D.C.
- 1949-1950 : Research Assistant, Institute of Research in Social Science, Chapel Hill, N.C.

MILITARY SERVICE
- 1944-1946 : Corporal, United States Army

HONORS AND OTHER SPECIAL RECOGNITION
- : Phi Beta Kappa
- : W.A. Jump Meritorious Award, 1960
- : DHEW Superior Service Award, 1973

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

IMPACT OF VACANCIES

Question: Dr. Malone, we know of 12 major vacancies at NIH. We, of course, know that Dr. James Wyngaarden, Chairman of the Duke University Medical School, has been nominated by the President to direct NIH. Do you anticipate filling the other vacancies in 1982?

Answer: It is expected that by the end of calendar year 1982, all these vacancies will be filled.

Question: To what extent has there been any effect on your day-to-day or long-term operations and planning abilities?

Answer: While some decisions have been delayed in deference to the individuals to be selected for these vacancies, administrative momentum has been maintained on most issues and operations. Therefore, the impact of the vacancies has been minimized.

NIH LIBRARY

Question: What is the relationship of the NIH Library to the National Library of Medicine? Do they duplicate, coordinate, overlap?

Answer: The NIH Library's collection of 60,000 current books and journals titles is small in comparison to the National Library of Medicine's million and one-half volume collection. Although the NIH collection duplicates in part materials on clinical medicine held by the National Library of Medicine, the scope of the NIH collection is much broader focusing on basic science, medical research, and allied fields. The NIH collection is accomodated in open-stacks and is circulated freely to the resident scientific community. The National Library of Medicine operates a closed-stack facility and access to the user is through the interlibrary loan mechanism.

The relationship of the NIH Library to the National Library of Medicine is essentially the same as any other medical/health sciences library to the National Library of Medicine. The National Library of Medicine has little direct-user involvement, working, instead, through a network of medical libraries across the nation to provide its information services. The NIH Library services its local clientele, and turns to the National Library of Medicine for loan of materials on medicine not owned by the NIH Library. The National Library of Medicine does not admit users to its stacks areas.

The NIH Library maintains an up-to-date collection with approximately one-half of the collection geared to the support of basic and applied research scientists who have diverse literature interest such as mathematics, chemistry, demography, space research, entomology, physics, and other disciplines outside the specific fields of medicine. The quality, location, and accessibility of the NIH Library in the Clinical Center is a major factor in the accreditation of the NIH hospital.

Whereas services of the National Library of Medicine are available nationally and internationally to medical professionals through a network of local medical libraries, the NIH Library is organized to immediately provide the requirements of a highly specialized and diverse research population. The NIH Library is a vital force in the NIH research effort as it integrates and tailors programs to the everchanging needs of the investigator by providing open-stack accessibility, facilities and service with proximity to the laboratories and offices of the scientific community, availability of a unique collection of scientific literature tailored to the NIH research programs, and special activities such as photocopying and translation services provided in a timely manner to the research staff.

Basically there is no overlap of effort between the two organizations. The NIH Library calls upon the resources of the National Library of Medicine to compliment or expand its information sources when required by the NIH scientific community.

BUILDINGS AND FACILITIES

Question: What accounts for the proposed $7.6 million increase in funding for Buildings and Facilities?

Answer: The $7.6 million increase consists of the following items: $5 million is for the first increment of rehabilitation of the old laboratory buildings 2,3,4,5,7 and 8; $1 million is for extension to Building 21 to provide additional handling capability for radioactive/hazardous chemical waste; $700,000 is for energy conservation modifications to Building 31; 300,000 represents an increase in the amount allocated this year for continuation of the modernization of the Clinical Center, for a total of $6.6 million; and $600,000 is the increase for the ongoing program of repairs and improvements to existing buildings and facilities for a total of $4.2 million.

Question: You not only want to rehabilitate the lab buildings, but you also propose "horizontal and vertical expansion"? Please explain.

Answer: Horizontal and vertical expansion applies only to Building 8. It is necessary to enlarge this building by about 20,000 net square feet at the outset in order to accomodate the programs now in Building 4. At the end of the cycle of renovating Buildings 2,3,4,5,7 and 8, we will then demolish Building 9, which will offset the increase in space to Building 8. Building 9 is not suitable for rehabilitation or continued long-term occupancy.

The funds requested this year of $5 million will permit the necessary expansion of the shell of Building 8, as well as demolition within the present building. We will require about $7 million next year to complete the renovation (installation of interior walls, utility systems, laboratory benches, etc.).

Question: What other projects could be deferred?

Answer: The rehabilitation of the older laboratory buildings has already been delayed for several years until other major construction projects on the NIH campus were completed. Further delays would subject us to unacceptable risks emanating from (1) the hazards to which the investigators are subjected in working in an environment that does not meet safety codes, and (2) the increasing probability of catastrophic failure of the support systems that would force a major disruption of on-going laboratory research. Likewise, modernization of the Clinical Center is urgently needed to overcome serious safety and program-related deficiencies. Interruption of this 10-year program would have serious consequences.

The other two projects for which funds are requested--expansion of radioactive and hazardous waste disposal facilities, and installation of sun screens and double glazing on windows in Building 31C--are expected to lead to substantial decreases in operating expenditures. The $1 million expansion of Building 21 will permit initiation of new procedures that will make possible substantial decreases in the costs of radioactive and hazardous waste disposal, now running $900,000 per year. The $700,000 to be spent on Building 31 is expected to lead to energy savings of about $184,000 per year. The funds requested represent support for only our very highest priorities, and we believe that it would be unwise to defer any of them.

Question: Please bring us up to date on the Clinical Center modernization, which this Committee has strongly supported.

Answer: This project is designed to correct safety deficiencies and functional obsolescence and to integrate the existing building with the new Ambulatory Care Research Facility (ACRF). Work is proceeding on schedule, and some aspects will be able to be accelerated as occupancy of the ACRF frees space that must be renovated in the main building. Thus far, more than $10 million has been obligated, with a number of major contracts soon to be awarded. Projects that have already been completed or are nearing completion include creation of a surgical intensive care unit, modernization of two patient care units, and renovations of the facilities for the Sterile Supply Unit and the Media and Glassware Section. Major projects that have recently started or are scheduled to begin soon include the creation of areas of refuge from fire on each floor, modernization of two patient care units, automation of the main elevator bank in the Clinical Center, and the installation of a "telelift" system to deliver supplies to the nurses' stations at the various patient care units.

In addition to the $6.6 million requested this year, we estimate that about $32 million (in 1983 dollars) will be required over the next five years to complete the modernization.

CLINICAL CENTER MODERNIZATION

Question: How much disruption of your research and patient care activities are you experiencing because of the modernization?

Answer: While some disruption to the research and patient care activities has been unavoidable, every effort has been made to minimize the risks, inconveniences and delays associated with the modernization effort. Containment of the disruption has been possible through a phased approach to the renovation and rehabilitation process. Although this approach results in a longer total period for the entire renovation effort, it facilitates the accomodation of hospital staff and routine to periods of alteration and change.

POSSIBLE CUTS IN OVERHEAD EXPENSES

Question: In light of current constraints on the budget, and the need to put adequate funds in research, what savings can you achieve in direct operations and program management in fiscal 1983?

Answer: The request for the Office of the Director includes a program decrease of $369,000 which will be applied to non-personnel areas such as equipment rentals and purchases, printing, training and small contracts. In addition to these specific budgetary savings, the NIH is participating in Department-wide studies and is conducting studies of its own, aimed at identifying overlap and inefficiencies, which will result eventually in broad-based administrative savings and overall systems improvements.

Question: What are your most important administrative concerns--and what are your least important concerns?

Answer: With regards to the Office of the Director, the overriding concern is managing available resources so as to maximize efficiency in operations. Within that broad context, concern exists for the maintenance of momentum on several initiatives, such as the full operation of the recently completed Ambulatory Care Research Facility and the new NIEHS facilities at North Carolina, and the further development and implementation of the NIH Administrative Data Base. Our least concern for the Office of the Director appropriation is in initiating new programs or expanding existing ones, provided this does not contradict or compromise mandated action or wise management.

Question: What criteria do you use for determining your administrative priorities?

Answer: In broad terms, the establishment of administrative priorities is guided by the requirements of law or regulation, Congressional, Departmental, and Presidential intent, sensitivities to public opinion, and the overall availability of resources. Within that framework, criteria are developed, specific to various issues and activities. A number of internal administrative groups have been established to assist the Director and Associate Director for Administration, NIH, in this effort.

IMPACT OF BUDGETARY RESTRICTIONS

Question: Are there any initiatives you would like to undertake which are not possible because of budgetary restrictions?

Answer: While there are a number of NIH-wide functions and programs which would benefit from additional staff and resources, it is possible to defer further emphases until the actual degree of budgetary flexibility is known.

Question: Will the present budget allow you to maintain existing programs and operations at an adequate level?

Answer: The FY1983 request will maintain the Office of the Director at its present level of operations.

PERSONNEL SERVICES

Question: The Direct Operations portion of the appropriation for the Office of the Director includes certain personnel services for over 11,000 NIH employees. How do your employees feel about the adequacy of the counseling, training, and other personnel services that you provide?

Answer: During the period from 1968 through 1979 several employee attitude surveys were administered at NIH in connection with PHS, DHHS, and Office of Personnel Management evaluations of our personnel management and equal employment programs. The survey results in each case reflected a generally positive attitude toward employment and management at NIH while also identifying some weaknesses in the provision of personnel services, particularly in the areas of communication with employees, supervisory training, and policy development. NIH responded to these findings first by providing staff for those programs that needed to be strengthened and then by a major reorganization of the personnel management function in 1980.

The Division of Personnel Management has lost approximately 25 positions since 1978. During this same period, the demands for communication with employees, supervisory training, and policy development have significantly expanded as a result of Civil Service Reform. Although we do not have any current data to indicate how employees perceive the personnel program, we know that we are not meeting the demand for services in these three areas and must asume that this is generating some employee dissatisfaction.

SUBCOMMITTEE RECESS

Senator RUDMAN. I believe, Dr. Malone, that we have finished with the battery of witnesses that you supplied today. We appreciate it very much.

The subcommittee will now stand in recess until 9:30 tomorrow morning when it will meet in room 1318 Dirksen to receive further testimony on the NIH.

[Whereupon, at 2:45 p.m., Monday, February 22, the subcommittee was recessed, to reconvene at 9:30 a.m. on Tuesday, February 23.]

LIST OF WITNESSES, COMMUNICATIONS, AND PREPARED STATEMENTS

Page
Amoruso, Philip D., Executive Officer, National Cancer Institute, Department of Health and Human Services ... 431
Ashbaugh, Richard R., Acting Director, Bureau of Medical Services, Health Services Administration, Department of Health and Human Services ... 139

Baldwin, Calvin B., Associate Director for Administration, National Institutes of Health, Department of Health and Human Services ... 371, 681
  Statement ... 685
Becker, Edwin D., Associate Director for Research Services, National Institutes of Health, Department of Health and Human Services ... 681
Bloom, James D., Executive Officer, Centers for Disease Control, Department of Health and Human Services ... 57
Bode, John, Deputy Assistant Secretary for Food and Consumer Services, Department of Agriculture ... 139
Brandt, Edward N., Jr., Assistant Secretary for Health, Department of Health and Human Services ... 11
Butler, Dr. Robert N., Director, National Institute on Aging, Department of Health and Human Services ... 585
  Statement ... 592

Carlos, Dr. James P., Associate Director, National Caries Program, National Institute of Dental Research, Department of Health and Human Services ... 527
Christiansen, Dr. Richard L., Associate Director, Extramural Programs, National Institute of Dental Research, Department of Health and Human Services ... 527
Cummings, Dr. Martin M., Director, National Library of Medicine, Department of Health and Human Services ... 663
  Statement ... 668

Denton, Jeremiah, U.S. Senator from Alabama ... 3
DeVita, Dr. Vincent T., Director, National Cancer Institute, Department of Health and Human Services ... 431
  Statement ... 432
Doak, William, Executive Officer, John E. Fogarty Center for Advanced Study in the Health Sciences, National Institutes of Health, Department of Health and Human Services ... 647
Du Buy, Yvonne H., Budget Officer, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services ... 219

Fitzsimmons, Executive Officer, National Institute of General Medical Sciences, Department of Health and Human Services ... 255
Foege, Dr. William H., Director, Centers for Disease Control, Department of Health and Human Services ... 57
  Statement ... 11, 59
Forbush, Wilford, Deputy Assistant Secretary for Health, Operations, Department of Health and Human Services ... 11

Page

Frommer, Dr. Peter L., Acting Director, National Heart, Lung and Blood Institute, Department of Health and Human Services 473
  Statement 476

Goggins, Dr. John F., Acting Director, National Institute of Dental Research, Department of Health and Human Services 527
  Statement 531
Goldstein, Dr. Murray, Acting Director, National Institute of Neurological and Communicative Disorders and Stroke, Department of Health and Human Services 189
  Statement 192
Graham, Robert, Acting Administrator, Health Resources Administration, Department of Health and Human Services 11

Hardy, Dr. George E., Jr., Assistant Director/Washington, Centers for Disease Control, Department of Health and Human Services 57
Hartinger, John P., Financial Manager, National Cancer Institute, Department of Health and Human Services 431
Hawkins, Paula, U.S. Senator from Florida, statement 8
Hedetniemi, Joel R., Executive Officer, National Institute of Child Health and Human Development, Department of Health and Human Services 283
Henney, Dr. Jane, Deputy Director, National Cancer Institute, Department of Health and Human Services 431
Hodgkins, Guy Earl, Budget Officer, National Institute of General Medical Sciences, Department of Health and Human Services 255

Itteilag, Anthony, Deputy Assistant Secretary, Budget, Department of Health and Human Services 57, 139, 189, 219, 255, 283, 307, 335, 371, 431, 473, 527, 549, 585, 617, 647, 663, 681

Jordan, Dr. Elke, Associate Director for Program Activities, National Institute of General Medical Sciences, Department of Health and Human Services 255

Kelso, John H., Acting Administrator, Health Services Administration, Department of Health and Human Services 139
  Statement 140
Kirschtein, Dr. Ruth L., Director, National Institute of General Medical Sciences, Department of Health and Human Services 255
  Statement 257
Krause, Dr. Richard M., Director, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services 219
  Statement 226
Kupfer, Dr. Carl, Director, National Eye Institute, Department of Health and Human Services 307
  Statement 310

Laurence, L. Earl, Executive Officer, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, Department of Health and Human Services 549
Leasure, Charles E., Jr., Executive Officer, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services 219
Lenfant, Dr. Claude J. M., Director, John E. Fogarty Center for Advanced Study in the Health Sciences, National Institutes of Health, Department of Health and Human Services 647
  Statement 653
Little, W. Harell, Deputy Associate Administrator for Management, Health Services Administration, Department of Health and Human Services 139

Page

Malone, Dr. Thomas E., Acting Director, National Institutes of Health, Department of Health and Human Services ... 189, 283, 307, 335, 431, 473, 527, 549, 585, 617, 647, 663, 681
  Statement ... 314
Mansfield, Norman D., Director, Division of Financial Management, National Institutes of Health, Department of Health and Human Services ... 219, 255, 431, 527
Martin, Dr. Edward D., Director, Bureau of Community Health Services, Health Services Administration, Department of Health and Human Services ... 139
Matthews, William, Budget Officer, National Institute of Neurological and Communicative Disorders and Stroke, Department of Health and Human Services ... 189
McManus, Edward, Deputy Director, National Eye Institute, Department of Health and Human Services ... 307
Mecklenburg, Marjory, Director, Office of Adolescent Pregnancy Programs, Office of the Assistant Secretary for Health, Department of Health and Human Services ... 11
Millar, Dr. John D., Director, National Institute for Occupational Safety and Health, Department of Health and Human Services ... 57
Moskowitz, Dr. Jay, Associate Director for Scientific Program Operation, National Heart, Lung and Blood Institute, Department of Health and Human Services ... 473

Nylen, Dr. Marie U., Director, Intramural Research, National Institute of Dental Research, Department of Health and Human Services ... 527

O'Donnell, Dr. James F., Acting Director, Division of Research Resources, National Institutes of Health, Department of Health and Human Services ... 617
  Statement ... 622

Patterson, John, Executive Officer, National Institute of Dental Research, Department of Health and Human Services ... 527
Pickelsimer, Claude F., Jr., Director, Financial Management Office, Centers for Disease Control, Department of Health and Human Services ... 57
Pickett, Dr. Betty H., Acting Director, National Institute of Child Health and Human Development, Department of Health and Human Services ... 283
  Statement ... 285
Press, Gilbert D., Budget Officer, National Institute of Dental Research, Department of Health and Human Services ... 527

Rall, Dr. David P., Director, National Institute of Environmental Health Sciences, Department of Health and Human Services ... 335
  Statement ... 338
Rall, Dr. Joseph E., Acting Deputy Director for Science, National Institutes of Health, Department of Health and Human Services ... 371
Raub, Dr. William, Associate Director for Research and Training, National Institutes of Health, Department of Health and Human Services ... 371
Ringler, Robert, Deputy Director, National Institute on Aging, Department of Health and Human Services ... 585
Rudman, Hon. Warren, U.S. Senator from New Hampshire, questions submitted by ... 657

Salans, Dr. Lester B., Acting Director, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, Department of Health and Human Services ... 549
  Statement ... 553
Sell, Dr. Kenneth, Scientific Director, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services ... 219
Shafer, Richard L., Executive Officer, Division of Research Resources, National Institutes of Health, Department of Health and Human Services ... 617
Smith, Kent A., Deputy Director, National Library of Medicine, Department of Health and Human Services ... 663

	Page
Talbot, Dr. Bernard, Deputy Director, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services	219
Von Euler, Dr. Leo H., Deputy Director, National Institute of General Medical Sciences, Department of Health and Human Services	255
Waugaman, Paul G., Executive Officer, National Institute of Environmental Health Sciences, Department of Health and Human Services	335
Whiteside, Dr. Daniel F., Director, BHPDS, Health Services Administration, Department of Health and Human Services	139

SUBJECT INDEX

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Page
Abortion referral ... 40
Adolescent:
  Family life ... 14
  Pregnancy prevention ... 17
  Programs aimed at males ... 20
Approaches to prevention ... 18
Area health education centers ... 26
Categorical grants for TB control ... 23
Demonstration benefits ... 37
Dissemination of information on adolescent family life demonstrations ... 15
Drug resistant tuberculosis ... 45
Education on tuberculosis and other health problems ... 23
Elderly care ... 27
Emergency response ... 32
  Capabilities ... 14
Federal tuberculosis assistance ... 46
General funding ... 39
Geriatric medicine training ... 49
HHS tuberculosis activities ... 44
Identification of cases of tuberculosis ... 24
Implementation of program ... 30
Incidence of tuberculosis among children ... 21
Introduction of associates ... 11
National Health Service Corps ... 32
Pacific Basin area aid ... 53
Parental consent ... 39
  Requirement ... 17, 36
PHS testing capabilities ... 33
Prevention services ... 36
Preventive health:
  Services block grant ... 22
  Strategies ... 28
Preventive medicine:
  Programs in medical school ... 30
  Residencies ... 30, 46
  Specialists ... 27
Primary care research and development ... 34
Public health emergency response fund ... 53
Research ... 37, 41
  Activities in adolescent health ... 19
Special health professions initiative ... 30, 48, 50
Submitted questions ... 35
Susceptibility to tuberculosis ... 22
Title X information and educational materials ... 41

Page
Training in:
  Geriatric medicine 26
  Preventive medicine 14
Tuberculosis:
  As a serious health problem 21
  Control 13, 42
    Program 20
  In refugees 43
  Transmission of 25

ADMINISTRATION

Age of passenger vehicles 683
Buildings and facilities 689
Clinical Center modernization 684, 690
Effect of continuing resolution 682
Impact of:
  Budgetary restrictions 691
  Vacancies 688
Introduction of associates 681
NIH library 688
Passenger vehicles 682
Personnel services 692
Possible cuts in overhead expenses 691
Questions submitted by the subcommittee 673
Rehabilitation of laboratory buildings 683

CENTERS FOR DISEASE CONTROL

Accountability 72
Advent of the Occupational Safety and Health Act (OSH Act) 97
Agent Orange 130
Alcohol and drug abuse 123
Appreciation of health problems 75
Birth defects 118
Block grant and Indian tribes 114
Block grant/program management 103
Block grants 71
Budget request 70
  To OMB 71
Buildings and facilities 126
Cancer 83
Childhood immunization 87
Clinical observation opportunities 74
Correcting misconceptions 100
Disease reoccurrence 80
Environmental hazards 92
Epidemic control 122
Epidemics 125
Fluoridation 90
Health:
  Education 73, 85
  Hazard evaluations 117
Herpes 89
Hospital infections 84
Immunization 75, 88
Infant mortality 102
Introduction of associates 58
Job stress 121

National Institute of Occupational Safety and Health (NIOSH): Page
    Creation of 97
    Documents 111
    Funds 131
    Move 96
    Projects 109
    Relocations 104
    Training 82, 102
    Transfer of Headquarters 81, 96
    OSHA/MSHA 137
Nutrition 80
    Surveillance and monitoring 95
Overview 68
Questions submitted by the subcommittee 85
Rationale 98
Risk reduction/health education 86
Stress and violent behavior 124
Superfund 94
Transfer authority 114
Transfer of Administration of block grants 85
Treatment-resistant VD 117
Tuberculosis 78
    Central TB and refugees 91
Venereal disease 115

HEALTH SERVICES ADMINISTRATION

1982 pay costs 183
Adolescent health 148, 162
Assistance to States under block grants 174
Birthing centers 185
Block Grant Administration 173
Block grants 160
Bureau of Community Health Services program support 148, 157, 168
Community health centers 149, 162
Exceptional financial need scholarships 152, 165, 184
Family planning 146, 150, 164, 176
    Research 179
Health education assistance loans (HEAL) 183
Health professions student loans 165
Health Services Administration:
    Program management 168
    Program support requirements 185
Loan defaults 153
Lobbying with Federal funds 185
Maternal and child health:
    Block grant 144, 158, 170
        Allocations 173
    Set-aside 148, 161
Medically underserved areas update 169
Migrant health 184
National Health Service Corps (NHSC) 181
    Loans 182
    Pay costs 183
    Physician supply 180
    Private practice option 180

Page

Nursing student:
  Assistance 156
  Loans and scholarships 166
Payment to Hawaii for treatment of Hansen's disease 188
Primary care:
  Block grant 146, 147, 159, 174
  Research and demonstration 150, 163
Public Health Service hospitals and clinics 156, 167
Questions submitted by the subcommittee 158
Reduction in scholarship-assignee pay 151
Services for women, infants and children block grant 145, 159
State Block Grant Administration 143, 534, 169
State block grant reporting 172
Submitted questions 157
Summary of statement 143
Updating medically underserved areas designations 169
Use of commercial collection agencies 154

NATIONAL INSTITUTES OF HEALTH

JOHN E. FOGARTY CENTER FOR ADVANCED STUDY IN HEALTH SCIENCES

Advanced international studies 653
Attendees at flu virus conference 650
Budget cutbacks 661
Conference in foreign lands 658
Contributions to Gorgas by other countries 650
Effect of continuing resolution 648
Flu virus conference 648
Funds for flu virus conference 650
General policy 661
Gorgas Memorial Institute funding level 659
Gorgas Memorial Laboratory 650
Information dissemination 660
International coordination and liaison 655
International research and awards 655
Language provision 659
Questions submitted by the subcommittee 652, 658
Response to budget constraints 648
Summary statement 647

DIVISION OF RESEARCH RESOURCES

Accomplishment of general clinical research centers program 619
Administrative overhead reductions 618
Automated mass spectrometer 632
Biomedical research support program (BRSP) 640
Biotechnology research centers 629
Black colleges 645
DRR planning activities 627
Effect of:
  Continuing resolution 618
  Indirect cost reduction 619
Extramural grant support 641
General clinical research centers 636, 640
Goals of the MBS program 644
Hiring freeze 627
Improvement of animal facilities 635
Introduction of associates 617
Live animals in research 640

Page
Minority apprenticeship program ... 641
Minority biomedical research support (MBS) program ... 636, 643, 637
  Status of ... 642
Primate:
  Breeding ... 620
    In the private sector ... 638
  Research ... 633
  Shortages ... 633
Projects with industry ... 630
Prophet computer network ... 620, 631
Questions submitted by the subcommittee ... 627
Recouping resource investments ... 619
Reductions in 1883 ... 628
Regional primate centers ... 637
Reorganization of DRR ... 629
Training in:
  Laboratory animal medicine ... 633, 638
  Veterinary medicine ... 621
Unfunded grant applications ... 644

NATIONAL CANCER INSTITUTE

Anticancer drugs ... 441
  Controversy ... 449
Biological response modifiers ... 469
Budget reductions ... 445
Cancer:
  Causes of ... 467
  Control ... 462
  Detection ... 464
  Investigations ... 438
  Treatment ... 466
Clinical trials ... 464
Community clinical oncology program ... 459
Fraud and abuse ... 460
Impact of budget reductions ... 440
Indirect costs ... 440
Informed consent ... 463
Interferon ... 442, 457
Introduction of associates ... 431
Lack of a Deputy Director ... 448
Naturally occurring anticancer agents ... 442
Pi-Meson technology in cancer treatment ... 443
Plant product collection ... 456
Possible cuts in overhead expenses ... 446
Prior particle ... 440
Research:
  Centers ... 445
  Efforts ... 438
  Recent advances ... 438
Research Modernization Act ... 470
Strides during previous 10 years ... 439
Submitted questions ... 444
Toxicity of cancer drugs ... 448
Transfer of national toxicology program ... 441
Transforming genes ... 468

NATIONAL EYE INSTITUTE

Page
Administrative priorities 325
Basic research in neurobiology 313
Cataract 328
Clinical trials 324
Construction 317
Corneal diseases 327
Fiscal year 1982 continuing resolution 321
Funds for construction in fiscal year 1982 321
Glaucoma 328
Grants reduction 323
Impact of planning: Uveitis research as an example 310
Implementation of construction program 319
Intramural program 324
Introduction of associates 307
Low vision and rehabilitation 329
Major studies underway 331
Man-made drugs 333
Marihuana for glaucoma 332
Nobel Prize winners supported by NEI 309
Obligation of construction funds 319
Planning for vision research 310
Possible cuts in overhead expenses 325
Prevention of:
    Disease 330
    Eye disease 311
Priorities outlines in 1983–87 program plan 316
Program development priorities fiscal year 1983–87 327
Program planning 307
Progress in other areas of clinical research 312
Research and training efforts 316
Research priorities 326
Retinal and choroidal disease 327
Sensory and motor disorders of vision 317
Strabismus, amplyopia, and visual processing 329
Submitted questions 322
Uveitis 308

NATIONAL HEART, BLOOD, AND LUNG INSTITUTE

Adult respiratory disease syndrome 506
Alcohol and cardiovascular disease 492
Artificial:
    Blood 494
    Heart 482, 500
Asthma 504
Blood research 507
Budget 497
    Cuts 481
    Policy 496
Cap on indirect costs 481
Cardiovascular:
    Mortality 473
    Risk factors 493
Chronic obstructive pulmonary disease 503
Clinical trials 524

Page

Coronary:
  Artery bypass surgery: Scientific and clinical aspects 484
  Artery surgery 482
  Bypass surgery 501
Cystic fibrosis 505
Diabetes 480
Disease prevention and health promotion 521
Emphysema 506
Environmental and occupational health research 504
Hypertension 515
  Therapies 518
Impact of continuing resolution 496
Introduction of associates 473
Major advances 474
National blood policy 514
Overview matters 523
Possible cuts in overhead expenses 499
Potential growth 495
Research centers 481
Serum cholesterol levels 519
Submitted questions 495
Training 517

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Ability to produce good science and researchers 234
Accelerated development of new vaccines 221
Allergy and asthma 251
Asthma and allergic diseases 229
Basic research 229
Biological revolution 220
Budget 240
Common gene material 233
Demand for trained researchers for industry and agriculture 234
Diseases of the immune system 228
Food alergy 252
Grants comparison 240
Hepatitis B vaccine 238
Hepatitis vaccine 251
Immunotherapy 246
Impact of:
  1982 continuing resolution 235
  Reductions in grants and training 234
Infectious diseases 226
Interferon 254
International biomedical research 244
Introduction and associates 219
Possible cuts in overhead expenses 243
Recombinant DNA Advisory Committee 245
Research centers 241
Response to directive on sexually transmitted diseases 236
Rocky Mountain laboratories 225
Sexually transmitted diseases 247
Status of interferon research 238
Submitted questions 239
Support for research on sexually transmitted diseases—STD 237, 238
Training 242
Tropical medicine and international health 227

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

Page
1982 reprograming 561
Arthritis 569, 578
  Research 560, 563
Artificial pancreas 571
  Development 563
Budget 568
  Policy 566
Calcium metabolism 559
Competing constituencies 574
Cystic fibrosis 573
Diabetes 570
  Coordination 573
Digestive diseases 582
Disease prevention 581
Gene splicing 580
Hodgepodge or logic? 580
Hypertension and kidney disease 577
Impact of:
  Budget 566
  Continuing resolution 566
Insulin and human growth hormone 576
Introduction of associates 549
Kidney stones 551
Morbid obesity 577
National Arthritis Commission recommendations 579
Possible cuts in overhead expenses 568
Program balance initiative 562
Request for Bureau status 560
Research centers 569
Rumored reprograming 568
Submitted questions 565
Training 575
Treatment of kidney disease 576
Vascular complications of diabetes 572

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Adolescent nutrition 304
Basic science 287
Birth control pill 291
Birth defects 285
Budget 305
  Request 288
Child nutrition 303
Diabetes 300
Future plans 288
Impact of:
  1982 continuing resolution 293
  Budget policies 293
Introduction of associates 283
Mental retardation 286
New budget 297
New contraceptive drug 300
Population research 299
Pregnancy research progress 283
Prematurity 285
Prevention 285

Page
Public information ... 305
Research centers ... 298
Select panel ... 298
Social and behavioral science ... 288
Submitted questions ... 296
Sudden infant death syndrome (SIDS) ... 302
Test tube fertilization ... 294, 301
Treatment in pregnancy ... 301

NATIONAL INSTITUTE OF DENTAL RESEARCH

Average cost of grants ... 540
Budget:
  Cuts ... 540
  Policy ... 543
Caries and consumer food items ... 544
Caries vaccine ... 537
Cleft lip and cleft palate ... 528
Clinical research ... 541
Constant dollars ... 538
Cost of periodontal disease treatment ... 539
Decrease in dental caries ... 538
Dental:
  Caries prevalence survey ... 528
  Materials ... 544
  Research institutes and centers ... 539
  Vaccines ... 546
Diabetes ... 543
Diet and dental caries ... 546
Indirect cost of research grants ... 536
Introduction of associates ... 527
Nutrition ... 536
Oral health research ... 529
Periodontal diseases ... 528, 538, 543
Possible cuts in overhead expenses ... 541
Prevention ... 542
Public information programs ... 542
Research centers ... 537, 540
Submitted questions ... 537
Substitute sweeteners ... 543
Water fluoridation ... 545

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Agent Orange ... 347
Carcinogenesis ... 362
Chemical waste ... 356
Cutbacks in environmental R&D ... 354
Environmental health issues ... 353
General Counsel's opinion ... 347
General policy ... 352
Impact of continuing resolution ... 350
Indoor air quality ... 367
Introduction of associates ... 335
NCI bioassy:
  Personnel ... 346
  Transfer ... 345
NIEHS research facility ... 369

Page
Phenoxy herbicides 367
Possible cuts in overhead expenses 350
Program planning 351
Projects of importance 354
Questions submitted by the subcommittee 350
Reductions in force 351
Research and training efforts 344
Research centers 351
Risk assessment 368
Teratogenesis 361
Toxic chemicals 358
Water quality 357

NATIONAL INSTITUTE OF GENERAL MEDICINE SCIENCES

Artificial skin 274
Biomedical engineering 273
Budget 279, 281
Cell research 278
Cellular and molecular basis of disease 258, 268
Continuing resolution impact 262
Dr. Kornberg's research 265
Effects of budget cuts 264
Fraud and abuse 267
Genetics 257, 270
Huntington's disease research 277
In-house training efforts 262
Indirect costs and trainee expenses 263
Introduction of associates 255
Minorty access to research careers (MARC) 259, 275
Pharmacological sciences 258
Pharmacology 272
Physiology and bioengineering 259
Polygenic diseases 276
Possible cuts in overhead expenses 267
Private sector funding 263
Progress in categorical areas 268
Research:
    And training cost controls 262
    Centers 280
    Training 259
Submitted questions 266

NATIONAL INSTITUTES OF HEALTH

Achievements 392
Audit review 408
Award rates and paylines 423
Biological revolution 378
Biomedical research training 413
Budget request 372
Capping indirect costs 415
Centers/intramural research 414
Changes of patent law 385
Clinical trials 424
Cost effectiveness 392
Cutting back programs 399
Diabetes initiative 388, 402

Page
Direct operations and program management 387
Director's Advisory Committee 404
Distribution of reductions to grantees 387
Drug development 404
Effect of marihuana smoking 380
Emerging technologies 403
General policy 407
Impact of:
    1982 continuing resolution 386
    Budget policies 383
Indirect cost containment 425
Indirect costs 410, 421
Inflation rate 386
Inflation/extramural costs 399
Information dissemination 399
Introduction of associates 371
Mismanagement and data falsification 412
National toxicology program 417
NIEHS construction funds 424
Percentage of approved grants 411
Private sector support 384
Progress and achievements 372
Proposed increase in grants 406
Prostaglandins 389
Protecting programs 396
Questions submitted by the subcommittee 391
Receptor sites 419
Reduction in indirect costs 428
Report on containment of indirect costs in research 426
Research:
    Grant reductions 425
    Projects 416
Research Modernization Act 416
Retention of screen tests 385
Risks of alcohol consumption 382
Surgeon General's report on smoking 379
Technology transfer 389
Trans-NIH issues 389

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Budget:
    Cuts 208
    Increase 207
Clinical:
    Research 209
    Trials 210
Epilepsy 213
Fiscal year 1983:
    Budget 199
    Cutback 199
Huntington's disease 210
Impact of:
    1982 continuing resolution 199
    Orphan Drug Act 197
Inflation 211
Introduction of associates 190

Page

NIH personnel ... 198
Orphan Drug Act ... 206
Orphan drugs ... 196
Other diseases ... 215
Program management ... 205
Project with industry ... 217
Reduction:
  In new grants ... 208
  Of new research grants ... 206
Research centers ... 200, 208
Special review ... 216
Spinal cord research ... 214
Stroke ... 213
Submitted questions ... 207
Summary of program ... 190
Technological development ... 205
Training increase ... 211

NATIONAL LIBRARY OF MEDICINE

Administrative savings ... 677
Benefits from MEDLARS III ... 678
Cataloging backlog ... 667
Effect of continuing resolution ... 664
Leasing of NLM data bases ... 673
MEDLARS:
  Evaluation studies ... 614
  Pricing ... 665
MEDLARS III ... 673
MEDLINE and MEDLARS ... 678
Medical library assistance program ... 677
NLM:
  Cataloging backlog ... 675
  Data base fees ... 672
Opening statement highlights ... 663
OTA report ... 679
Questions by the subcommittee ... 672
Regional libraries ... 676
Research programs ... 679
Tape licensing agreements ... 666

NATIONAL INSTITUTE ON AGING

Alzheimers disease ... 589, 598
Areas of progress ... 587
Average lifespan ... 588
Budget reductions ... 607
Care of the elderly ... 603
Clinical Center ... 606
Coordination of nutrition research ... 614
Fraud and abuse ... 600
Geriatric medicine ... 587, 609
Grants comparisons ... 603
Impact on continuing resolution ... 590
Introduction of associates ... 587
Life span ... 596
NIH appointments ... 586
Nutrition and the elderly ... 612

Page
Questions submitted by the subcommittee 596
Research:
  Centers 612
  Grants 607
Senile dementia 599
  Initiative 606
Shortage of geriatricians 603
Teaching nursing homes 590, 601

O